The Oxford Medicine

BY VARIOUS AUTHORS

VOLUME VI

EDITED BY

HENRY A CHRISTIAN A M M D LL D Sc D (Hon) M A C P
Hon F R C P (Can) D S M (A M A)

Hersey Professor of the Theory and Practice of Physic Emeritus Harvard University
Sometime Clinical Professor of Medicine Tufts College Medical School
Sometime Visiting Physician Beth Israel Hospital
Physician in Chief Emeritus Peter Bent Brigham Hospital Boston Mass

NEW YORK
OXFORD UNIVERSITY PRESS
1949

PRINTED IN THE UNITED STATES OF AMERICA

CO-EDITORS

BURGESS GORDON, M.D.

Clinical Professor of Medicine, Jefferson Medical College; Director and Physician in Chief, Barton Memorial and White Haven Divisions, Jefferson Hospital, Philadelphia, Pennsylvania

WILLIAM J. KERR, M.D.

Professor of Medicine, University of California Medical School; Physician in Chief, University of California Hospital, San Francisco, California

CYRUS C. STURGIS, M.D.

Professor of Medicine, University of Michigan; Director, Thomas Henry Simpson Memorial Institute for Medical Research; Chairman, Department of Internal Medicine, University Hospital

CONTRIBUTORS TO
VOLUME VI

N S ALCOCK MD
Director, Royal Cornwall Infirmary Truro England

WALTER C ALVAREZ MD
Professor of Medicine Mayo Foundation University of Minnesota Head of Section and Senior Consultant, Division of Medicine Mayo Clinic Rochester Minn

A GREIG ANDERSON MD FRCP (Lond)
Formerly Assistant Physician Aberdeen Royal Infirmary Aberdeen Scotland

CARL BINGER MD
Assistant Professor of Clinical Psychiatry Cornell University Medical School Associate Attending Psychiatrist New York Hospital New York N Y

W RUSSELL BRAIN DM (Oxf) FRCP (Lond)
Physician Royal London Ophthalmic Hospital and Hospital for Epilepsy and Paralysis Maida Vale Neurologist Mount Vernon Hospital London England

GORONWY BROUN MD
Professor of Internal Medicine St Louis University School of Medicine Physician and Medical Director of the Out Patient Department St Louis University Hospital Group Consultant Physician St Louis City Hospital St Louis Mo

SIR E FARQUHAR BUZZARD Bart KCVO MD LLD FRCP (Lond)
Late Regius Professor of Medicine University of Oxford Late Extra Physician to H M the King Consulting Physician to St Thomas's Hospital London Late Hon Physician to the Radcliffe Infirmary Oxford, England

HARRY CAMPBELL MD BS FRCP (Lond)
Late Physician Hospital for Diseases of Nervous System and West End Hospital London England

HILDRED CARLILL, M.D., M.A. (Cantab.)
Formerly Physician to Westminster Hospital and Lecturer on Diseases of the Nervous System in the Medical School, Sometime Physician to the West End Hospital for Nervous Diseases, etc., London, England

STANLEY COBB, M.D.
Bullard Professor of Neuropathology, Harvard University; Chief of Service, Psychiatry, Massachusetts General Hospital, Boston, Mass.

JAMES COLLIER, M.D., B.Sc., F.R.C.P. (Lond.)
Late Consulting Physician and Emeritus Lecturer in Neurology, St. George's Hospital; Late Senior Physician, National Hospital for Paralyzed and Epileptic, London, England

D. DENNY-BROWN, M.D., Ch.B., Dr. Phil., F.R.C.P. (Lond.)
Professor of Neurology, Harvard University; Director, Neurological Unit, Boston City Hospital, Boston, Mass.

F. GOLLA, M.D., F.R.C.P. (Lond.)
Director of Burden Neurological Institute; Formerly Professor of Pathology of Mental Disorders, University of London; Director, Maudsley Hospital, London; Formerly Physician, Hospital for Epilepsy and Paralysis; Formerly Physician, St. George's Hospital, London, England

A. H. GORDON, M.D., C.M., F.R.C.P. (Can.)
Professor of Medicine Emeritus, McGill University; Consulting Physician to the Montreal General Hospital, Montreal, Canada

C. PHILIP GRABFIELD, M.D.
Formerly Instructor in Pharmacology, Harvard University; Formerly Associate in Medicine, Peter Bent Brigham Hospital; Milton, Mass.

SAMUEL B. GRANT, M.D.
Instructor in Clinical Medicine, Washington University; Assistant Physician in Medicine, Barnes Hospital, St. Louis, Mo.

BERNARD HART, M.D.
Physician in Psychological Medicine, University College Hospital, London, and National Hospital, Queen's Square, London; Lecturer in Psychiatry, University College Hospital Medical School, London, England

C M HINDS HOWELL DM (Oxon) FRCP (Lond)
Physician National Hospital for Paralysis and Epilepsy Queen's Square London Consulting Physician St Bartholomew's Hospital London England

REDVERS IRONSIDE MB FRCP (Lond)
Neurologist to West London Hospital Physician, Hospital for Paralysis and Epilepsy Queen's Square, London, Physician to London Hospital, London, England

WILLIAM G LENNOX MD SD
Assistant Professor of Neurology and Secretary of Harvard Epilepsy Commission Harvard University Boston Mass

WARFIELD T LONGCOPE MD LLD DSc (Hon)
Professor of Medicine Emeritus Johns Hopkins University Formerly Physician in Chief Johns Hopkins Hospital Baltimore Md Cornhill Farm Lee Mass

SIR ASHLEY W MACKINTOSH KCVO MD FRCP (Edin)
Late Emeritus Professor of Medicine Aberdeen University Late Consulting Physician Aberdeen Royal Infirmary Aberdeen, Scotland

J PURDON MARTIN MA MD FRCP (Lond)
Neurologist British Post Graduate Medical School Physician to Out Patients National Hospital for Nervous Diseases Queen's Square, London, England

DONALD McEACHERN MD
Biological Chemist Montreal Neurological Institute Lecturer in Neurology McGill University Montreal, Canada

H HOUSTON MERRITT MD
Professor of Clinical Neurology College of Physicians and Surgeons Columbia University Chief of Neuropsychiatric Division Montefiore Hospital New York N Y

SIR FREDERICK W MOTT KBE MD LLD FRS FRCP
Late Pathologist to the London County Asylums and Director of the Pathological Laboratory Late Physician to the Maudsley Neurological Hospital Denmark Hill Late Consulting Physician to Charing Cross Hospital London, England

DONALD MUNRO, M D

Assistant Professor of Neurological Surgery, Harvard University, Visiting Surgeon for Neurosurgery, Boston City Hospital, Boston Mass

J M NIELSEN MD

Associate Clinical Professor of Neurology, University of Southern California Los Angeles Cal

HAROLD D PALMER MD

Late Associate in Psychiatry Medical School, University of Pennsylvania Late Psychiatrist to the Institute of the Pennsylvania Hospital Philadelphia Pa

WILDER PENFIELD MD DSc (Oxon) FRCS (Can), FRCS (Lond) FRS

Director Montreal Neurological Institute Professor of Neurology and Neurosurgery McGill University, Montreal, Canada

TRACY J PUTNAM MD

Formerly Professor of Neurology and Neurological Surgery, Columbia University Formerly Director of Services of Neurology and Neurosurgery Neurological Institute New York, N Y Chief and Attending Surgeon Department of Neurosurgery Cedars of Lebanon Hospital Los Angeles, Cal

GEORGE RIDDOCH MD FRCP (Lond)

Physician and Director of Neurological Department to the London Hospital Physician to Out Patients the National Hospital for Nervous Diseases Queens Square, London, England

THURSTON D RIVERS MD

Assistant Psychiatrist the Institute of the Pennsylvania Hospital, Philadelphia Pa

T A ROSS MD FRCP (Edin) FRCP (Lond)

Late Medical Director Cassel Hospital of Functional Nervous Disorders Swaylands Penshurst Kent England

PERCY SAUNDERS MB, FRCP (Lond)

Formerly Assistant Physician National Hospital for Paralyzed and Epileptic and to the Royal Free Hospital London England

HARRY C SOLOMON MD

Professor of Psychiatry Harvard University Medical Director Boston Psychopathic Hospital Boston Mass

T GRAINGER STEWART MD FRCP (Lond)

Consulting Physician to the National Hospital for Paralysis and Epilepsy Queens Square London Formerly Consulting Neurologist, West London Hospital Consulting Neurologist to the Ministry of Pensions London England

EDWARD A STRECKER AM MD ScD (Hon) LittD (Hon)

Professor of Psychiatry School of Medicine University of Pennsylvania Chief of Clinic and Consultant to the Pennsylvania Hospital and the Institute of the Pennsylvania Hospital Philadelphia Penn

H CAMPBELL THOMSON MD FRCP (Lond)

Formerly Consulting Physician to the Department for Nervous Diseases Middlesex Hospital Formerly Consulting Physician to the Hospital for Epilepsy and Paralysis Maida Vale England

I S WECHSLER MD

Professor of Clinical Neurology Columbia University Attending Neurologist and Chief of Service Mt Sinai Hospital New York N Y

C WORSTER DROUGHT MD FRCP (Lond)

Consulting Physician in Neurology Bethlehem Royal Hospital Physician West End Hospital for Nervous Diseases London England

DONALD MUNRO, M D

Assistant Professor of Neurological Surgery, Harvard University, Visiting Surgeon for Neurosurgery, Boston City Hospital, Boston, Mass

J M NIELSEN M D

Associate Clinical Professor of Neurology, University of Southern California Los Angeles, Cal

HAROLD D PALMER M D

Late Associate in Psychiatry Medical School, University of Pennsylvania Late Psychiatrist to the Institute of the Pennsylvania Hospital Philadelphia Pa

WILDER PENFIELD M D D Sc (Oxon) F R C S (Can) F R C S (Lond) F R S

Director Montreal Neurological Institute Professor of Neurology and Neurosurgery McGill University Montreal, Canada

TRACY J PUTNAM M D

Formerly Professor of Neurology and Neurological Surgery, Columbia University Formerly Director of Services of Neurology and Neurosurgery, Neurological Institute New York, N Y Chief and Attending Surgeon Department of Neurosurgery Cedars of Lebanon Hospital Los Angeles, Cal

GEORGE RIDDOCH M D F R C P (Lond)

Physician and Director of Neurological Department to the London Hospital Physician to Out Patients the National Hospital for Nervous Diseases Queen s Square London, England

THURSTON D RIVERS M D

Assistant Psychiatrist the Institute of the Pennsylvania Hospital, Philadelphia Pa

T A ROSS M D F R C P (Edin) F R C P (Lond)

Late Medical Director, Cassel Hospital of Functional Nervous Disorders, Swaylands Penshurst, Kent England

PERCY SAUNDERS M B F R C P (Lond)

Formerly Assistant Physician National Hospital for Paralyzed and Epileptic and to the Royal Free Hospital London, England

ADDITIONAL CONTRIBUTORS TO VOLUME VI

CHARLES BRENNER M D

Associate in Neurology College of Physicians and Surgeons Columbia University Associate Attending Physician, Montefiore Hospital, New York City

KEITH S GRIMSON M D

Professor of Surgery Duke University School of Medicine and Duke Hospital Durham North Carolina

GORDON E. HEIN M D

Clinical Professor of Medicine University of California Chief of Medical Service Veterans Hospital San Francisco California

JAMES C REAVIS M D

Clinical Instructor in Medicine, University of California and Stanford University Attending Physician Veterans Administration Hospital, San Francisco, California

ROBERT F WATSON M D

Associate Professor of Medicine, Cornell University Medical College Attending Physician, New York Hospital Chief of Service The Vincent Astor Diagnostic Service New York City

CONTENTS OF VOLUME VI

CONTENTS OF VOLUME VI

CONTENTS

ADDITIONAL CONTENTS OF VOLUME VI

CONTENTS

ADDITIONAL CONTENTS OF VOLUME VI

CHAPTER I

ANATOMICAL AND PHYSIOLOGICAL INTRODUCTION TO DISEASE OF THE NERVOUS SYSTEM

By J. M. NIELSEN

TABLE OF CONTENTS

synaptic transmission is chemical but all the details of the nerve impulse itself are not entirely understood The action current in a nerve is a wave of negativity and activity is associated with a flow of ions The nerve impulse propagates itself along the nerve fiber Conduction is accompanied with a consumption of oxygen and liberation of carbon dioxide and heat The axon is a protoplasmic core surrounded by a membrane which lies in tissue fluid The membrane is relatively resistant to passage of ions in and about the membrane and there are ions on both sides of it If an impulse travels it is a maximum one nerve fibers like muscle fibers obey the all or none law The impulse is propagated as an active chemical phenomenon Adrian says The nerve impulse is a little patch of surface leakage spreading along the fiber and being sealed up again as soon as it is formed A breakdown of phosphocreatins and perhaps of phospholipins occurs The muscles receive a volley of impulses at the rate of 50 to 90 per second from each neuron Because of polarization at the synapse impulses normally travel in only one direction from the cell body down the axon The speed of conduction along the axon varies according to the size of the axon speeds of 80 to 120 meters per second are common in the human subject

At the synaptic junction and perhaps all along the axon acetylcholine is liberated as the nerve impulse passes This substance has a powerful and rapid stimulating action on the end plate region of the muscle and is rapidly hydrolyzed by an enzyme cholinesterase concentrated at or near the end plates The rapidity and chemical specificity of the acetylcholine effect suggest that acetylcholine produces its polarizing action by combining with specific chemical receptors on the surface of the muscle fiber Adenosinetriphosphate is the specific chemical substance involved in the generation of muscular energy

The neuronal cell bodies or perikaryons form the bulk of the cortex of the cerebrum and cerebellum the gray matter of the corpus striatum the thalamus all nuclei including the nuclei of the cranial nerves the gray matter of the spinal cord and the ganglia of the vegetative nervous system Myelinated processes of the ganglion cells form the bulk of the white matter of the brain and spinal cord and the sheathed neurons of the peripheral nerves Inasmuch as a single neuron probably never acts alone the reflex arc consisting of two or more neurons becomes the functional unit of neuronal physiology

Reflex Arc

The simplest reflex arc such as a segmental reflex arc of the spinal cord consists of a receptor a sensory (bipolar) neuron a synapse and the motor nerve to the *effector* (Fig 1) It is probable that an intercalated neuron a third neuron is present always even in the simplest reflex arc The motor neuron with it

The following outline of the anatomy and physiology of the nervous system is to be regarded merely as a statement of the fundamentals, which are necessary equipment to an understanding of the diseases affecting it An attempt is made to present what may be called the *present general concept* without entering into the history of its development

Neuron Doctrine

A basic concept of the neurophysiology is the neuron doctrine which originated with His and Forel and ripened with Ramon y Cajal[1] and Waldeyer, the last named gave the neuron its name The neuron doctrine states that the unit of neural function is the neuron or ganglion cell with its dendrites and axon and that all processes of the cell end without anastomosis or continuity with any other nerve cell but terminate by contiguity

A neuron consists of a cell body or perikaryon, filled with nucleus nucleolus and many ramifying fibrils and processes of two types dendrites which receive afferent impulses carried to the cell and an axon which transmits efferent impulses from the cell to another nerve cell or to an effector organ Normally impulses travel in only one direction The points of contact between two neurons is known as a synapse, the terminal fibrils of the axon have " end feet ' or buttons, boutons terminaux which contact the perikaryon or the dendrites of another neuron The neurons are held in a neuroglial mass of cells of three general types, astrocytes, oligodendroglia and microglia cells

The neurons are the conductors of the nerve impulses the astrocytes are attached with sucker feet to capillaries and have a supporting and nutrient function, the cells of the oligodendroglia take part in myelin formation the microglia cells are part of the reticuloendothelial system and hence are migratory and phagocytic

Inasmuch as the neuron is the unit of neuronal function and the synapse is the point of junction of neurons if one understands the anatomy and physiology of chains of neurons and knows not only the minute details of physiology but the gross function of all neuronal complexes as these function in groups for the benefit of the organism, one understands the entire groundwork of sensation, motor function emotions thoughts conditioned reflexes knowledge wisdom and psychology All functions of the central and peripheral nervous system as well as of the vegetative nervous system depend on the function of the neurons on the conduction of impulses We must therefore, know something of the nature of the nerve impulse

There has been a tremendous amount of study devoted to the question whether the nerve impulse is primarily electrical or chemical It has been settled that the

synaptic transmission is chemical but all the details of the nerve impulse itself are not entirely understood The action current in a nerve is a wave of negativity and activity is associated with a flow of ions The nerve impulse propagates itself along the nerve fiber Conduction is accompanied with a consumption of oxygen and liberation of carbon dioxide and heat The axon is a protoplasmic core surrounded by a membrane which lies in tissue fluid The membrane is relatively resistant to passage of ions in and about the membrane and there are ions on both sides of it If an impulse travels it is a maximum one nerve fibers like muscle fibers obey the all or none law The impulse is propagated as an active chemical phenomenon Adrian says The nerve impulse is a little patch of surface leakage spreading along the fiber and being sealed up again as soon as it is formed A breakdown of phosphocreatins and perhaps of phospholipins occurs The muscles receive a volley of impulses at the rate of 50 to 90 per second from each neuron Because of polarization at the synapse impulses normally travel in only one direction from the cell body down the axon The speed of conduction along the axon varies according to the size of the axon speeds of 80 to 120 meters per second are common in the human subject

At the synaptic junction and perhaps all along the axon acetylcholine is liberated as the nerve impulse passes This substance has a powerful and rapid stimulating action on the end plate region of the muscle and is rapidly hydrolyzed by an enzyme cholinesterase concentrated at or near the end plates The rapidity and chemical specificity of the acetylcholine effect suggest that acetylcholine produces its polarizing action by combining with specific chemical receptors on the surface of the muscle fiber Adenosinetriphosphate is the specific chemical substance involved in the generation of muscular energy

The neuronal cell bodies or perikaryons form the bulk of the cortex of the cerebrum and cerebellum the gray matter of the corpus striatum the thalamus all nuclei including the nuclei of the cranial nerves the gray matter of the spinal cord and the ganglia of the vegetative nervous system Myelinated processes of the ganglion cells form the bulk of the white matter of the brain and spinal cord and the sheathed neurons of the peripheral nerves Inasmuch as a single neuron probably never acts alone the reflex arc consisting of two or more neurons becomes the functional unit of neuronal physiology

Reflex Arc

The simplest reflex arc such as a segmental reflex arc of the spinal cord consists of a receptor a sensory (bipolar) neuron a synapse and the motor nerve to the *effector* (Fig 1) It is probable that an intercalated neuron a third neuron is present always even in the simplest reflex arc The motor neuron with it

termination in the muscle or gland commonly is called a motoneuron Receptors are of various types each with a special function Naked nerve endings serve for sensitivity to pain, Meissner s corpuscles for touch, Pacinian corpuscles for deep pressure Krause s end bulbs for cold Ruffini s end organs for warmth and so forth The retina serves for sensitivity to light the organ of Corti for sound, tactile hairs in the bulbs of the semicircular canals for movement of the endolymph,

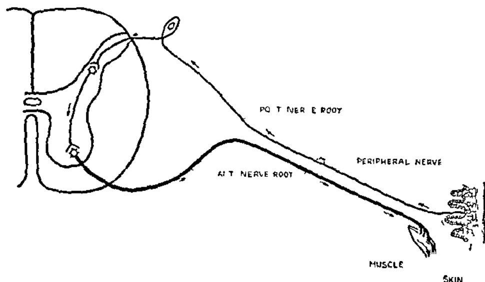


FIG 1 Diagram of the simplest spinal reflex arc of three neurons Skin is illustrated as the source of the afferent impulse the impulse may originate in muscle or tendon (Modified from Purves Stewart Oxford Medicine Chapt 1 Vol vi Oxford Univ Press New York 1926)

olfactory epithelium for smell and taste buds for taste If any stimulus is sufficiently intense pain results

A distinction should be made between perception of pain and the attitude of the individual toward it that is to say the emotional reaction One can be trained to a certain extent to have emotional reaction to pain those who suffer a great deal over a long period of time become inured to it although there is no evidence that the pain receptors are in any way altered The Amerindian is proverbially stoic pampered persons are plaintive Besides the element of training there is a constitutional element members of certain families have no emotional reaction to pain although they perceive it In one family under the observation of the writer two girls could be operated upon without anesthetic while a brother was so exquisitely sensitive that a casual contact with another person in passing on

the street made him wince and often weep with pain Two other families of persons insensitive to pain have been encountered

As stated above synap es are polarized impulses normally travel in only one direction from the dendrite to the cell body and from the body through the axon By artificial stimulation of a peripheral nerve the nerve impulse may be made to travel in either direction but not across a synapse Impulses can be summated in a reflex center but not in a fiber thus a subliminal stimulus if repeated may accumulate at the cell body until the threshold is crossed Variations in strength of stimuli cause a corresponding gradation in reflex response not that impulses vary in strength in a given fiber but that more fibers may take part if the stimulus is stronger Furthermore an ineffectual stimulus causes a central excitatory state in the ganglion cell in such a manner that subsequent stimuli may rise above the threshold value If the same stimulus is merely continued, *recruitment* may cause activity in more motoneurons and thus give rise to reflex action

The simplest reflex arc as stated involves two neurons It is however rather the exception than the rule to have a two neuron reflex As stated even the simplest spinal reflexes generally involve an intercalated neuron The great majority of reflexes involve *chains of neurons*

The great master of neurophysiology Sherrington as recorded in his book The Integrative Action of the Nervous System showed in experimental work on dogs that the spinal cord separated from the higher levels was capable of a remarkable degree of integration The general law was established that an irritation produces a *movement* not a muscular contraction Now as it is well known that nearly all muscles in the body are supplied from three successive segments of the spinal cord it must be clear that an impulse entering through a single segment spreads up and down the cord to stimulate *at the very least* anterior horn cells in *three segments* However inasmuch as antagonistic muscles in any movement must be inhibited to allow orderly contractions of the protagonists there must be present in the spinal cord a coordination mechanism an integration pattern to cause simultaneous stimulation in one group of muscles and inhibition in another Sherrington showed that there are segmental and intersegmental spinal reflexes

Examination of the spinal cord shows that there are short ground bundles of white fibers immediately applied to the gray matter These bundles serve for coordination within the spinal cord The white matter as seen on cross section evidently is nearly as voluminous for these ground bundles as for all of the long fiber tracts

Types of Spinal Reflexes

Flexor Reflex — This spinal reflex is the most primitive of all It consists of a flexion withdrawal of a limb from a noxious stimulus The reflex is more

violent from an irritation of the skin than it is from stimulation of deep sensory nerves It represents a defense mechanism against nociceptor stimuli Literally thousands of neurons must take part in such a coordinated movement which flexes hip knee ankle and sometimes digits The ganglion cells of the cord "seem to think", inasmuch as a useful purpose is served by the reflex However, since the reflex centers have no choice the reflexes are clearly inherited functional pattern acquired by millenniums of usage

The clinical importance of the flexor reflex is widespread It is the basic cause of doubling up in acute abdominal disease in sciatica and as Fulton[4] points out probably in arthritis When the clinician elicits a Babinski sign he must always guard against accepting the general flexion movement as a positive sign The examiner's stimulus must be graded to fit the sensitivity of the sole of the foot and the mass flexion is wisely avoided or prevented by the examiner during the test

Stretch Reflex — Sherrington discovered the extension reflexes in decerebrate dogs They depend on the stretch reflex the receptor end organ of which is the muscle spindle found in the red muscle fibers This reflex acts selectively upon antigravity muscle and is the basic reflex for posture Simply stated the stretch reflex is elicited in an appropriate muscle simply by stretching it very slightly the muscle then contracts and remains in tonic contraction for a long time fatigue hardly occurs

Through the work of Denny Brown now of Harvard University, and many investigators prominent among which are the physiologists of Yale University it has become the modern concept that the red muscle fibers occurring in various muscles are the ones serving chiefly in maintenance of posture and that the muscles with such fibers are the ones which become rigid in reflex standing They particularly resist the effects of gravity By the universal law of reciprocal innervation by which through spinal coordination the antagonists are inhibited when certain muscles are stimulated the flexors are coordinated with the extensors in the extensor reflex Decerebrate rigidity is reflex standing

In the intact animal and in the human subject it is clear that reflex posture is modified by higher centers particularly the cerebral cortex There is a certain correlation possible which the writer has not seen in the literature but which seems suggestive that normal standing and walking are normally relatively free from cortical control The generally accepted basic facts which do not seem to require proof and from which a corollary can be drawn are as follows

1 A normal person stands and walks with an habitual pattern not requiring attention unless external factors bring about necessity for change

2 Habitual acts which no longer require attention are integrated in the basal ganglia particularly the putamen and globus pallidus with their lower connections — the red nucleus corpus subthalamicum and reticular formation

3 In paralysis agitans in which the disease process affects the projection fiber system of the globus pallidus reflex standing and walking are particularly disturbed The disease produces festination and abnormal postures with weakening of the antigravity muscles The normal postures and normal walking can be carried out if the patient uses his cortex to think out what needs to be done However, since normal walking usually is not thought out the walking which thus is cortically managed is a caricature of the normal

Intersegmental Reflexes —The intersegmental reflexes have already been mentioned By virtue of these the well known scratch reflex of the decerebrate dog or frog enables the animal to scratch the appropriate spot with the hind foot when the skin of the trunk is irritated There are also positive and negative supporting reactions in the dog whose spinal cord is isolated from the brain These are illustrated by extension of the limbs of the side toward which the standing dog is gently pushed and relaxation of the opposite limbs This reflex serves an obvious purpose and makes cerebral guidance of posture unnecessary under such circumstances in the normal animal

There are also visceral segmental reflexes These include engorgement of the genitalia with assumption of the characteristic copulation posture when the perineum is stimulated The bladder and rectum will empty reflexly when a certain degree of distension of the viscera has been attained A mass reflex is evoked also by appropriate stimuli this results from a diffusion of the impulses in the cord and may cause in addition to the reactions just described also sweating and rise of blood pressure These reactions are seen in a modified degree in man after recovery from spinal shock in cases of transection of the cord

Final Common Pathway

The anterior horn cells of the spinal cord the lower motor neurons are not mere passive ganglion cells subject to reflex action They are small coordinating centers themselves They receive all of the reflex stimuli described above for final transmission to the effectors but they receive also a tremendous flux of impulses from higher centers in the intact animal or human being They receive impulse from (Fig 2) (1) the cortico spinal tracts (pyramidal tract and prepyramidal pathways) (2) the rubrospinal tract (3) the reticulospinal tract (4) the tecto spinal tract (5) the vestibulospinal tract (6) the ground bundles from other levels of the spinal cord (7) proprioceptive and exteroceptive impulses reflexly

The anterior horn cells are played upon by all these sources of stimuli and must accept reject and modify these impulses and pass on to their axons the algebraic sum of all of them in the best interests of the organism It is for this reason that Sherrington called the lower motor neuron the final common pathway

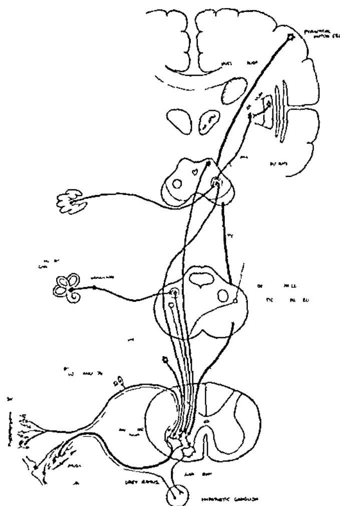


Fig 2 Diagram to show the sources from which impulses converge on the anterior cornual cell Py pyramidal tract T S tectospinal tract R S rubro pinal tract D R dentatorubral tract V S vestibulospinal tract The cell out of place on the border of the anterior horn represents a lateral cornual cell of the sympathetic system (Redrawn from Purves Stewart Oxford Medicine Chapt I Vol vi Oxford Univ Press New York 1926)

Lesions of the Lower Motor Neuron

The "lower motor neuron lesion is a concept of great value to clinical neurology Inasmuch as the cell body of the neuron in the anterior horn of the spinal cord or in the brain stem for the homologous cranial nerves is the nutrient center for the axon degeneration of the cell body will cause degeneration of the entire axon and section of the axon will cause degeneration of the entire peripheral end Furthermore the lower motor neuron is the trophic mechanism necessary for preservation of the muscle fibers supplied by it Incidentally the synaptic boutons of other neurons ending at the anterior horn cell will degenerate if the cell body is damaged

When a motor nerve is cut the nerve beyond the section will undergo degeneration simultaneously all along its course The myelin sheath will disintegrate into droplets and will disappear gradually as the products are absorbed by scavenger cells Each cut axon also will degenerate centrally to the first node of Ranvier The cells of the neurolemma will proliferate This form of degeneration is known as Wallerian degeneration named for Waller who first described it As regeneration takes place new fibers are generated at the rate of ½ to 4 mm a day according to whether the channels are well apposed or not and according to other favorable or unfavorable circumstances

The symptoms of degeneration of a set of lower motor neurons in the spinal cord assuming a considerable number to render the symptoms clinically identifiable as in chronic anterior poliomyelitis are as follows (1) flaccidity of muscles ( ) loss of reflexes (3) fibrillation or fasciculation in the affected muscle fibrillae or fa ciculi (4) degeneration of the motor end plates in the muscles (5) atrophy of the affected muscles (6) reaction of degeneration (R D) and increase in the chronaxia (7) contracture in antagonists of the affected muscles

As nearly every voluntary muscle in the body is supplied by three successive motor roots the section of a single root will cause atrophy and fasciculation only in the muscle fascicles supplied by that root However not all fasciculation is of central origin Damage to the neuromuscular end plates will cause it al o Hence it is correct to state that damage to any portion of the lower motor neuron may cause fasciculation — even excessive fatigue or interference with the blood supply of a muscle

Lower Sensory Neuron

The lower sensory neuron has its cell body in the posterior root ganglion Its peripheral fiber begins in a receptor in the skin tendon or muscle The central fiber ends in the gray matter of the spinal cord posterior horn region or in the nuclei gracilis and cuneatus The distribution of the cutaneous fibers of a nerve

are quite different from the distribution of the radicular fibers because each nerve especially in the limb region passes through a plexus and sends its component fibers to the spinal cord through several roots The section of Oxford Loose Leaf Medicine on the peripheral nerves must be consulted for the cutaneous distribu

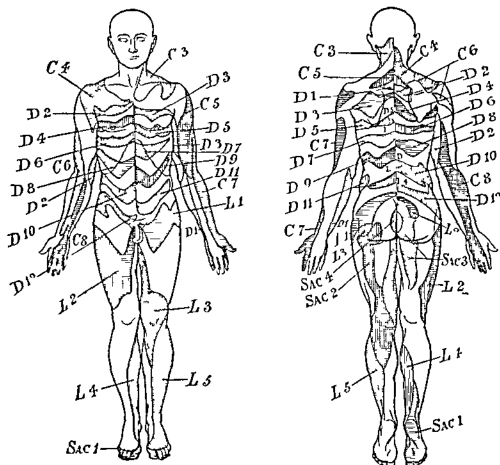


FIG 3 Photograph of Henry Head's dermatomes based on lesions of herpes zoster Brain xxiii 1900

tion of the various nerves here will be explained the manner of cutaneous distribution of the fibers in roots

The first great principle is that the dermatomes overlap Head worked out a most intricate distribution for each root based on the cutaneous lesions in cases of herpes zoster (Figs 3, 4a, 4b and 5) in which the posterior root ganglia are the seat of infection The enormous advances of neurosurgery have made available innumerable cases of section of individual roots done for various rea

sons It has been found that the section of a single root gives a variable but remarkably limited loss of sensory perception best tested by sensitivity to pin prick. This method gives for each root only the area of skin supplied exclusively by that root but as the adjoining roots supply overlapping areas, the actual extent of sup-

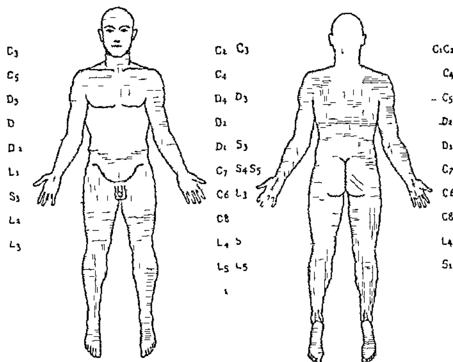


Fig 4 Radicular distribution of cutaneous areas simplified for practical diagnostic purposes (From Nielsen Textbook of Clinical Neurology Hoeber New York 1941)

ply of a root is not thus determined If on the other hand the roots above and below a given root are sectioned the area of retained sensibility is much larger because the overlap of that dermatome on the others is included The chart shown is a working system to which while no specific case may absolutely conform any case will conform sufficiently to be of clinical application

are quite different from the distribution of the radicular fibers because each nerve especially in the limb region passes through a plexus and sends its component fibers to the spinal cord through several roots The section of Oxford Loose Leaf Medicine on the peripheral nerves must be consulted for the cutaneous distribu

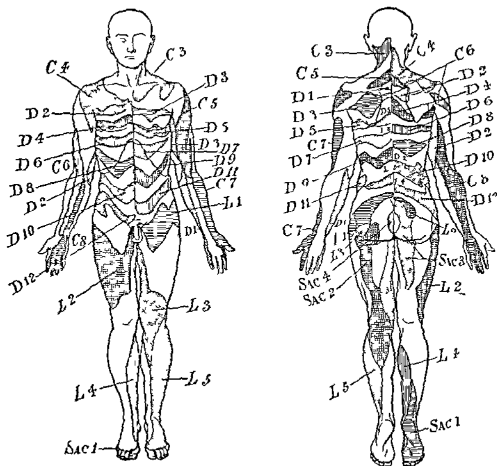


Fig 3 Photograph of Henry Head's dermatomes based on lesions of herpes zoster Brain xxiii 1900

tion of the various nerves here will be explained the manner of cutaneous distribution of the fibers in roots

The first great principle is that the dermatomes overlap Head worked out a most intricate distribution for each root based on the cutaneous lesions in cases of herpes zoster (Figs 3 4a 4b and 5) in which the posterior root ganglia are the seat of infection The enormous advances of neurosurgery have made available innumerable cases of section of individual roots done for various rea

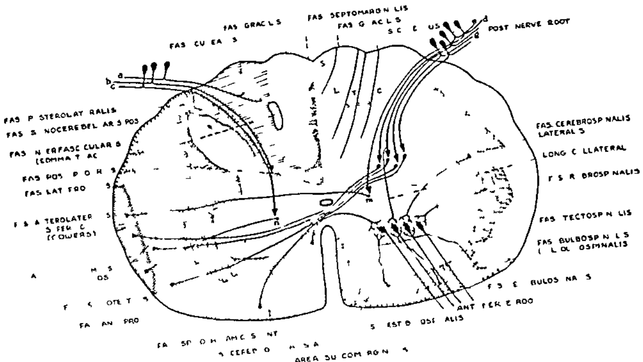


FIG 6 Gross tracts of pinal cord diagrammatic (Redrawn from Elliot Smith Cunningham s Anatomy Wm Wood New York)

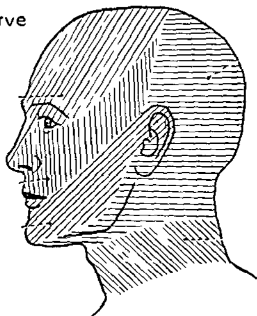


FIG 5 Trigeminal and radicular distribution to head and neck (From Nielsen Textbook of Clinical Neurology Hoeber New York 1941)

GROSS ANATOMY OF THE SPINAL CORD

The spinal cord extends from the medulla oblongata to its termination between the first and second lumbar vertebrae from which point the filum terminale extends to the tip of the coccyx It lies ensheathed in pia mater and arachnoid with a relatively large intermediary subarachnoid space in which the cerebrospinal fluid is found Outside the arachnoid is the dura mater Between the latter and the spinal column is a pad of epidural fat The spinal cord hangs relatively free in the subarachnoid space reaching as stated in the adult to a point between the first and second lumbar vertebrae Below this point the cauda equina is found, in that area spinal punctures can be done without trauma to the cord

The spinal cord consists of a core of roughly H shaped gray matter with a tiny central canal surrounding all of which are tracts of white matter (Fig 6) The cross sectional appearance is only crudely H formed and it varies greatly at vari

chain through the white ramus communicans If it is destined to return it re enters through the gray ramus to be distributed with the spinal nerves The gray matter contains the bodies of the neurons whose axons are to form the peripheral motor nerves It also contains intercalated neurons which serve to form multiple connections of one axon of a fiber tract (of the white matter) or of one sensory fiber entering through the posterior horn with many motor neurons In this way the gray matter acts as a great coordinating center for segmental and inter segmental reflexes as already outlined

The white matter consists of fiber tracts Those which immediately adjoin the gray matter are short or long ground bundles of association tracts uniting neurons of various segments for coordinated action Long fiber tracts conveying impulses down from the brain or up to it lie slightly farther from the gray matter Between the posterior horns are the two tracts of Goll and Burdach gracilis and cuneatus which convey proprioceptive impulses upward to the nuclei of the same names at the lower border of the medulla Up to the level of those nuclei the fibers are uncrossed i e they convey impulses from the same side of the body The fibers from the lower part of the body are placed close to the midline septum and as the fibers enter from higher levels these take places more laterally In the upper part of the cord the fibers from the upper limbs thus are placed nearer the posterior horn of the gray matter These fibers convey impul es conveying perception of position and vibration and some impulses of tactile perception It is not the same fibers which convey each form of sensation but different ones all are variously susceptible to disea e and toxins in such a manner that clinically any form of perception may be lost without the other

The clinical application of these facts is that tactile sensation as well as sensa tions of vibration and position are uncros ed a unilateral lesion of the cord causes loss of such perception below the lesion on the same side

The spinothalamic tracts are organized quite differently The tracts are placed laterally just anterior to the midline as seen on cross section Their fibers are re ceived from the opposite posterior roots after crossing in the gray commissure The fibers are located in a laminated system those from the lowest levels being antero lateral the higher levels of the sensation (from the upper limbs) are located postero medially This fact is of great clinical importance because chordotomy for relief of intractable pain can be done in the latero anterior aspect for relief of pain in the lower limbs without a deep incision which might impinge upon the pyramidal tract

The corticospinal tract pyramidal tract which arises in the precentral gyrus of the opposite frontal lobe forms this tract after its passage down the internal capsule cerebral peduncles mesencephalon pons and medulla (Fig 8) The crossing occurs in the lower part of the medulla and the tracts take their places

ous levels As the large bodies of motor neurons lie chiefly in the anterior horns these horns are large at the levels at which any large nerves or plexuses are to be formed at the cervical and lumbar enlargements The increased size of the gray matter causes a general swelling in the cord at those levels The blood supply is shown in Fig 7

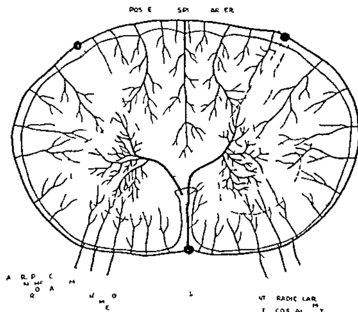


Fig 7 Blood supply of spinal cord (schematic)

The nerve roots, which form the connections between the spinal cord and the peripheral nerves are two in number at each segment, one anterior motor root and one posterior sensory root The cell body of the anterio root lies in the an terior or ventral horn of the gray matter the cell bodies of the posterior root lie in the ganglia which occur on each just central to the point of junction of the two roots to form a nerve After the two roots have united a single nerve is formed, which may then continue as such or may enter a plexus for more efficient distribu tion of the nerve fibers according to requirements of the limb musculature

Emerging from the spinal cord with the anterior root is a sympathetic neuron with cell body in the lateral horn of the spinal cord It follows the anterior horn to a point outside the spinal foramen and then makes its exit to the sympathetic

just behind the midline as seen on a cross section They lie between the ground bundles mesially and the posterior spinocerebellar tracts laterally

The physiology of this tract has been considered understood for many decades we are just discovering that our supposed knowledge was largely false It has been conventional to state that they were *the* motor tracts for voluntary motion that they conveyed the chief impulses required for voluntary activation of the anterior horn cells and that they *suppressed reflex activity* of those cells

However through the brilliant experimental operations on chimpanzees by Rothman Marshall and especially by Sarah Tower and Marion Hines* and by occasional natural experiments in the human subject it has been found that section of the the pyramidal tracts causes weakness rather than paralysis and that those tracts stimulate rather than inhibit the activity of the lower motor neurons Instead of increasing the deep reflexes section of the pyramidal tract diminishes them These revolutionary findings now undeniable compel us to revise our concepts

The modern concept is that the extrapyramidal tracts (frontal extrapyramidal rubro spinal reticulospinal tecto spinal vestibulospinal) and the ground bundles are capable of considerable voluntary action Moreover it is damage to elements of the extrapyramidal fibers which causes an increase in the deep reflexes and inhibition of the superficial ones in cases of upper motor neuron lesions It is damage to extrapyramidal fibers which causes spasticity paralysis of the pyramidal tract causes flaccidity which however is less marked than the flaccidity due to a lower motor neuron lesion The cause of the Babinski sign is *still* considered as heretofore a lesion of the pyramidal tract

The symptoms of upper motor neuron disease for practical purposes are still as they have conventionally been (1) increase of the deep reflexes (2) diminution of the superficial reflexes (3) spasticity with contractures (4) absence of atrophy except such as results from disuse (5) appearance of the Babinski sign or its equivalents

One must merely keep in mind that the upper motor neuron is not merely the neuron of the pyramidal tract

"Centers" in the Spinal Cord

A center in the sense in which the term is used in this article is not a compact group of cells anatomically delimited but a group of cells closely grouped or diffusely associated for the performance of a given function and whose destruction is recognizable by symptoms In this sense there are centers in the lumbo sacral spinal cord for control of bladder and rectal functions These centers after infancy are normally under voluntary control to a certain extent but if the viscera

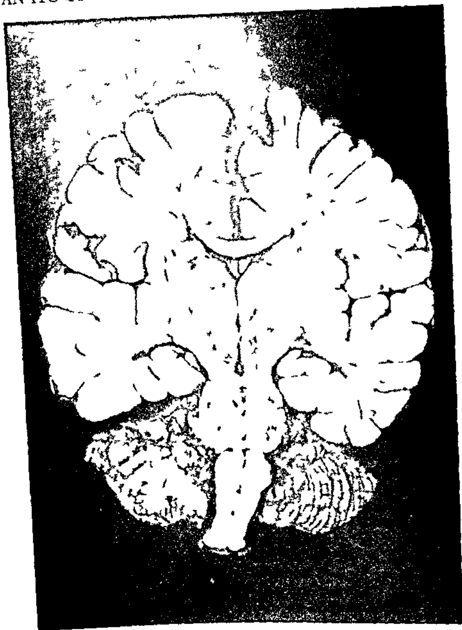


Fig 8 Untouched photograph of author's section through the pyramidal tracts of human brain The tract can be traced from the cortex through the internal capsule (between the thalami medially and the lenticular nuclei laterally) through the cerebral peduncles between the internal capsule and the pons through the pons and medulla oblongata In the medulla the decussation of the pyramidal tracts can be seen

limb may be seen before the paralysis develops In such cases the sphincters remain under voluntary control because the centers in the lumbosacral cord are innervated bilaterally

Medulla Oblongata

While the medulla oblongata is traversed by important ascending and descending tracts which do not have synapses there it is besides the seat of centers of vital importance to the organism In the lower portion is found the 'respiratory center The delineation of the center is not exact in man although in the cat an inspiratory and an expiratory center have been demonstrated In man the respiratory center is located at the calamus scriptorius

Anatomically it is a matter of highest importance that the cells constituting this center are located on both sides of the midline and that the two halves are united so intimately with association fibers that destruction of one pyramidal tract above the medulla does not deprive the individual of his usual voluntary control over both sides Another anatomical fact of vital importance is that the cells are not lower motor neuron cells they belong to the intercalated system and constitute a coordinating mechanism for the anterior horn cells which function in respiration

The respiratory center may be used as a paradigm for supranuclear coordinating mechanisms in general of which there are many There is one in the region of the mesencephalon just anterior to the superior colliculi whose function it is to coordinate extraocular muscle nuclei for the function of upward and downward gaze and one for convergence of the eyes There are others in the lumbosacral cord for coordination of sphincteric control Still another governs action of the abdominal and cremasteric muscles In the pons is found another for coordination of the upper facial muscles In short there are supranuclear coordinating mechanisms for all truncal structures which must function only in pairs

The respiratory center is the most highly developed of all these mechanisms and has a separate humeral control Even when it is deprived of all pyramidal innervation as in cases of decerebrate rigidity or in severe cases of amyotropic lateral sclerosis the respiratory center continues to function in response to the CO tension of the blood It also responds to reflex stimuli to function in reflex coughing and sneezing Thus in cases of pseudobulbar palsy when the patient has lost voluntary ability to hold his breath to cough to sigh or to sneeze the center will enable him to do all those things reflexly He holds his breath to evacuate his bowels he hiccoughs if the diaphragm is irritated he coughs if particles get into his larynx he sneezes if his nose is tickled In cases of bulbar palsy in which the nuclei of the hypoglossal nerves and other nuclei in the bull

in question are overdistended or if they are separated (by organic lesions) from higher control they escape such control and act to a certain extent automatically In the same sense there are diffuse "centers" or mechanisms associated with fiber tracts, for coordinated movements of flexion or extension of the lower limbs In certain ecstatic states such movements come into play

The clinical importance of such mechanisms some of which have been described already is their display in cases of section of the spinal cord If the spinal cord of a human being is severed suddenly as by a bullet or a knife there supervenes immediately a state of "spinal shock" due partly to the suddenness of isolation and partly to vasomotor paralysis If the section is acute, but less sudden, as in cases of transverse myelitis the symptoms of spinal shock are present but somewhat less marked In general the higher the level of the lesion the more severe the symptoms

In such cases the reflexes all disappear deep and superficial below the lesion The bladder and rectum empty themselves periodically involuntarily and without the patient s knowledge There is a strong tendency for extensive trophic lesions of the skin to develop, and only meticulous care will prevent ascending urinary infection and decubitus ulcers

A lesion of the third or fourth cervical segment will destroy the center for diaphragmatic control and hence will cause acute paralysis of the diaphragm Also it will cause priapism, as a rule in the male Hyperthermia sometimes results from a high cervical lesion, although the mechanism is not understood

At the first and second cervical segments is located another center an organization of cells made up of intercalated neurons which function in tonic neck reflexes The function of this center will be clarified when the medulla oblongata is discussed

In cases of slowly developed lesion of the cord such as caused by a neoplasm the symptoms can be studied in greater detail At first there is weakness of the lower limbs this is followed soon by spasticity Then the bladder sphincter is difficult to relax and distension with overflow appears By that time obstipation is evident The Babinski sign or its equivalent develops and we have a case of spasticity in extension the lower limbs are difficult to flex next flexor spasms appear followed by flexion contractures of the lower limbs and complete loss of control of the sphincters We now have spasticity in flexion a sign that the spinal cord is essentially severed

In cases of severance of one *lateral half of the* spinal cord there is loss of tactile and proprioceptive sensation with loss of voluntary motion on the same side below the lesion and loss of temperature and pain perception of the opposite side This is known as a Brown Séquard syndrome In slowly oncoming lesions as from compression *by a unilateral neoplasm all of the signs of* spasticity of the ipsilateral

and with the fastigial nuclei in the roof of the fourth ventricle (Fig 9) These nuclei are part of the paleocerebellar structure as is the flocculonodular lobe The vestibular nuclei have further important connections with the posterior longitudinal bundle median longitudinal fasciculus which is the most important association tract between the nuclei of nerves supplying the extraocular muscles The vestibular nuclei especially Deiters nucleus give rise to the vestibulospinal tract whereby the trunk and limbs respond to vestibular reaction Finally there is a direct connection with the neck muscles whereby movements of the head alone may respond to vestibular impulses

Tonic labyrinthine reflexes have their greatest influence through the utricular stimuli affecting the tone of the entire musculature Even when tonic neck reflexes are excluded (by section of all the uppermost afferent roots or by encasing the neck in a plaster cast) an extensive influence on the antigravity muscles is found The greatest extension effect is obtained when the animal is supine with snout at 45 degrees above the horizontal Minimal effect is obtained at a point after rotation about a transverse axis when the snout is 45 degrees below the horizontal level

Through connections of the vestibular nuclei with the centers for tonic neck reflexes these latter are influenced by the vestibular reactions There are also labyrinthine righting reflexes by which the head is held as much as possible in its proper relation to the level of the earth but the righting reflexes all operate through the midbrain The pathway is from the vestibular nuclei to the cerebellum thence by way of the superior cerebellar peduncles to the red nuclei and downward through various mesencephalic spinal tracts Labyrinthine ocular reflexes function through the posterior longitudinal bundles

Nystagmus while usually considered pathological is useful normally to permit ocular fixation on an object during head movements for example to permit a dog to keep its eyes on a rabbit while the positions of the head and body are constantly changing or to permit watching of passing game without necessitating movement of the head The mechanism fatigues with long use as every traveller has experienced in watching objects from a train

Destruction of one labyrinth causes skew deviation of the eyes the ipsilateral eye being directed downward the contralateral upward Destruction of the vestibulo cerebellar connections may produce a similar syndrome

The vestibulo spinal tract is essential to the tonic neck reflexes of Magnus and de Kleyn (see Fulton) as seen in decerebrate rigidity When fully developed these reflexes are as follows

Rotation of the head to the right causes the right limbs to go into extensor rigidity while the left limbs flex Flexion of the head to the side produces the same effect but usually to a less marked degree Rotation to the opposite side

degenerate, the respiratory center does not undergo degeneration, because it belongs as stated to the intercalated or internuncial neuronal system

Of extreme importance to an understanding of equilibrium in general specifically to equilibrium of the head and eyes and in relation to bodily posture and eyes are the vestibular nuclei These nuclei are located laterally in the medulla

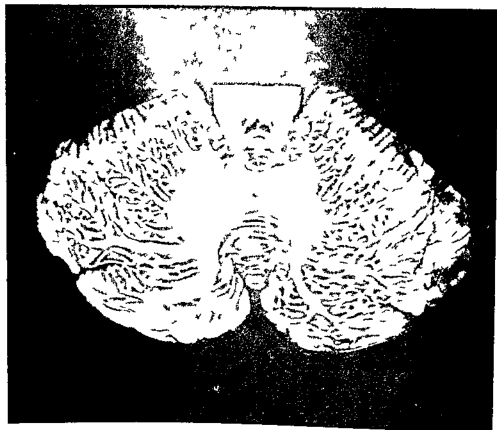


Fig 9 Horizontal section of the cerebellum to show the actual relationship of the fastigial globose and emboliform nuclei (Section made by Clemon Marsh)

and extend dorsally into the walls of the fourth ventricle The labyrinth consists of two physiologically different mechanisms the static utricle and saccule and the kinetic semicircular canals

The vestibular nuclei receive their impulses from the periphery by way of the vestibular nerves from the labyrinths Scarpa s ganglion in the course of the nerve is homologous with a posterior spinal root ganglion The vestibular nuclei also have important connections with the flocculonodular lobe of the cerebellum

and with the fastigial nuclei in the roof of the fourth ventricle (Fig 9) These nuclei are part of the paleocerebellar structure as is the flocculonodular lobe The vestibular nuclei have further important connections with the posterior longitudinal bundle median longitudinal fasciculus which is the most important association tract between the nuclei of nerves supplying the extraocular muscles The vestibular nuclei especially Deiters nucleus give rise to the vestibulospinal tract whereby the trunk and limbs respond to vestibular reaction Finally there is a direct connection with the neck muscles whereby movements of the head alone may respond to vestibular impulses

Tonic labyrinthine reflexes have their greatest influence through the utricular stimuli affecting the tone of the entire musculature Even when tonic neck reflexes are excluded (by section of all the uppermost afferent roots or by encasing the neck in a plaster cast) an extensive influence on the antigravity muscles is found The greatest extension effect is obtained when the animal is supine with snout at 45 degrees above the horizontal Minimal effect is obtained at a point after rotation about a transverse axis when the snout is 45 degrees below the horizontal level

Through connections of the vestibular nuclei with the centers for tonic neck reflexes these latter are influenced by the vestibular reactions There are also labyrinthine righting reflexes by which the head is held as much as possible in its proper relation to the level of the earth but the righting reflexes all operate through the midbrain The pathway is from the vestibular nuclei to the cerebellum thence by way of the superior cerebellar peduncles to the red nuclei and downward through various mesencephalic spinal tracts Labyrinthine ocular reflexes function through the posterior longitudinal bundles

Nystagmus while usually considered pathological is useful normally to permit ocular fixation on an object during head movements for example to permit a dog to keep its eyes on a rabbit while the positions of the head and body are constantly changing or to permit watching of passing game without necessitating movement of the head The mechanism fatigues with long use as every traveller has experienced in watching objects from a train

Destruction of one labyrinth causes skew deviation of the eyes the ipsilateral eye being directed downward the contralateral upward Destruction of the vestibulo cerebellar connections may produce a similar syndrome

The vestibulo spinal tract is essential to the tonic neck reflexes of Magnus and de Kleyn (see Fulton) as seen in decerebrate rigidity When fully developed these reflexes are as follows

Rotation of the head to the right causes the right limbs to go into extensor rigidity while the left limbs flex Flexion of the head to the side produces the same effect but usually to a less marked degree Rotation to the opposite side

produces the opposite effect. Flexion of the head forward causes the upper limbs to flex, the lower to extend. Pressure on the vertebra prominens causes relaxation of all limbs. In the human subject these reflexes are rarely completely developed, but if the clinician will study his cases carefully, he can often detect at least a lessening tone of the limbs toward which the occiput is turned and an increase in the others. This fact is of considerable value in diagnosis of compression of the brain stem or of hemorrhage into it.

Also located in the medulla are the nuclei of the vagus nerves with their important influence on the cardiac rate and upon blood pressure. Compression of the medulla causes first slowing of the pulse rate to a certain point. The cardioinhibitory mechanism finally fails and the heart races to an uncountable rate until the heart ceases entirely. The respiratory mechanism does not behave in the same way; respiration becomes slower and slower until it ceases.

In the lower portion of the medulla are located the nuclei gracilis and cuneatus, the first synaptic site for the proprioceptor fibers from the posterior root ganglia. Leaving the nuclei the arcuate fibers descend (go forward) and cross in the sensory decussation (above the motor), sending their fibers to the lateral nucleus of the (contralateral) thalamus.

Pons

The pons or bridge is essentially a mass of gray matter made up of nuclei, whose axons pass into the cerebellar hemisphere, and of smaller nuclei constituting the recticular formation of the pontine tegmentum (Fig. 10). This mass of gray matter is traversed by the fibers of the pyramidal tract, the rubrospinal tract, the tectospinal tract, the central tegmental fasciculus and the fibers of the retriculospinal system. Terminating in it are the fibers of the frontopontine and temporopontine tracts. All tracts ascending from the spinal cord to higher centers traverse the pons. The posterior longitudinal bundle and the corpus trapezoides are structures of importance for coordination of eye movements and for hearing respectively.

Located close to the nuclei of the sixth cranial nerves is a center of intercalated neurons for coordination of lateral gaze. The effect of a lesion in this center is to prevent movements to one side with a resultant fixation of the eyes away from the lesion.

Cerebellum

Through the work of Larsell the functional organization of the cerebellum seems finally to have been elaborated to the satisfaction alike of zoologists, embryologists, anatomists, physiologists and clinicians. The cerebellum develops as an outgrowth from the medulla oblongata, especially from the vestibular group of

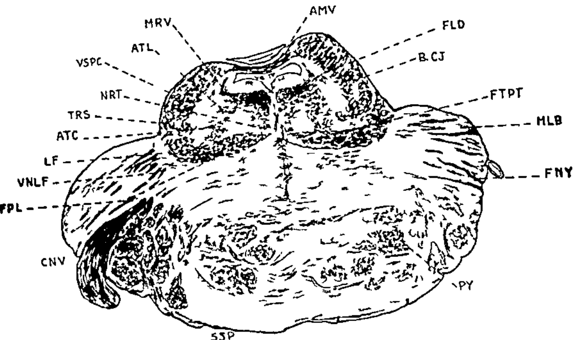


FIG 10 Author s drawing of myelin sheath section through the pons MRV mesencephalic root of the fifth nerve ATL area tegmenti lateralis VSPC ventral spinocerebellar tract NRT nucleus ruber tegmenti TRS tractus rubro spinalis ATC area tegmenti centralis LF lateral fillet VNLP ventral nucleus of lateral fillet FPL fasciculi pontini lateralis CNV trigeminal nerve AMV anterior medullary velum FLD fasciculus longitudinalis dorsalis B CJ brachium conjunctivum FTPT fasciculus temporo pontini tegmentalis MLB median longitudinal bundle FNY fibers of fifth nerve PY pyramidal tract SSP stratum superficialis pontini

nuclei It is primarily concerned with elaboration of vestibular mechanisms and hence of equilibrium The paleocerebellum still is concerned with those functions while the relatively enormous hemispheres which constitute the neocerebellum, are concerned with coordination of limb movements The two sets of function may be discussed separately

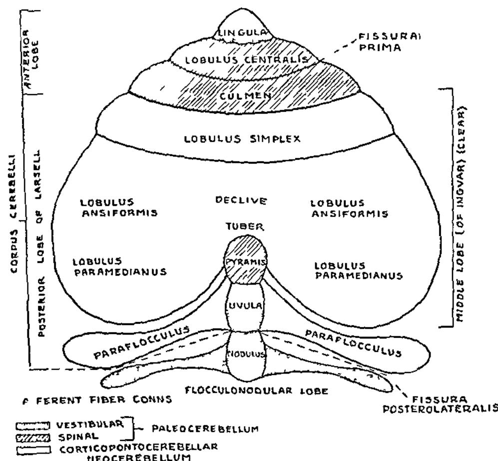


FIG 11 Scheme of the cerebellum according to Larsell and Dow (Redrawn from Fulton Physiology of the Nervous System Oxford Univ Press New York 1943)

The paleocerebellum consists of the anteriorly placed lobules the lingula, centralis and culmen and the posteriorly placed pyramis uvula and flocculonodular lobe (Fig 11) Of these the lingula uvula and nodulus have vestibular connections the others spinal The vestibular nuclei also have important connections with the fastigial globose and emboliform nuclei

From extirpation experiments it has become clear that the removal of the flocculonodular lobe and not of any other part of the cerebellum causes isolated disturbances of equilibrium i e disturbances without volitional tremor or alteration of reflexes This conception is entirely substantiated by clinical experience in that the common medulloblastoma of childhood which arises from that lobe gives precisely such symptoms

Furthermore it is known that after destruction of the labyrinths extirpation of the flocculonodular lobe does not cause additional symptoms The dentate nuclei and the main body of the hemispheres are constituents of the neocerebellum The afferent fibers of the dentate nuclei are from the Purkinje cells of the lobes the efferent fibers pass upward through the superior cerebellar peduncles some to others through the red nucleus Those which terminate there end in part in the magnocellular in part in the parvocellular nucleus Those which pass through end in the lateral part of the lateral nucleus of the thalamus After another relay fibers terminate in the frontal cortex areas 4 and 6 of Brodmann According to Fulton[4] this projection contributes little to the influence of the rubro spinal tract, as its chief termination is in the parvocellular nucleus and thence to the cerebral cortex However I believe with Spatz that the central tegmental fasciculus which arises from the red nucleus and descends into and through the entire tegmental reticular formation and into as well as past the inferior olive by relays reaches the ground bundles of the spinal cord and has a tremendous influence on posture in a completely unconscious manner

A point of prime importance in all cerebellar connections is that because of double decussation of all connections the cerebellar influence is ipsilateral to the cerebellar lobe Stimulation of the anterior paleocerebellum causes inhibition of ipsilateral antigravity muscles The neck and each limb have individual representation

In man the neocerebellar structure is far larger than the paleocerebellar and hence it must be considered important functionally It is related to the limbs in contrast to the paleocerebellum which is of principal importance for the trunk Ablation of the neocerebellar structure especially when the dentate nucleus is involved causes errors in force and rate of movements also errors in range and direction of movements Hypotonia is an enduring symptom in man after cerebellar destruction

Of great importance in man is the compensation made by the cerebral cortex for cerebellar destruction Surgeons do not hesitate to remove portions of the lobes in an approach to deeper structures and the general rule applies that unless a lesion of the cerebellum is progressive the patient overcomes the symptoms of cerebellar deprivation Bailey has shown an ontogenetic relation between the frontal lobe and the contralateral cerebellar lobe

Innumerable efforts have been made to summarize the function of the neo cerebellum in a single word The nearest approach to success in that effort is the word synergy the term for symptoms of deprivation is asynergy This word means without working together and applies to muscular function

It will be recalled that the principle of reciprocal innervation is ascribed mainly to the spinal cord that is to say patterns in the spinal cord cause the antagonists of any group of muscles to relax when the muscles in question con tract That the cerebellum also functions in this way is evident from the dis turbance of reciprocal innervation which appears when a progressive lesion of the cerrebellum occurs for example in the disease known as olivo ponto cerebellar atrophy or in a hereditary cerebellar ataxia However, once any disease of the cerebellum becomes stationary the spinal mechanisms are almost self sufficient in managing reciprocal innervation

Mesencephalon
(Midbrain)

The mesencephalon is a small portion of the brain stem only three quarters of an inch in length between the pons below and the hypothalamus above It contains structures of vital importance to the ' power plant ' of the individual inasmuch as destruction of the periaqueductal gray matter removes all tendency to spontaneous movement from the individual (cats and chimpanzee experiments, Bailey and Davis[8]) and the centers for waking and sleep are partly located there Anatomically it includes the cerebral peduncles the entrance of the superior cerebellar peduncles into the brain stem the corpora quadrigemina the red nuclei the substantia nigra and the third and fourth cranial nerve nuclei It is the center of the mesencephalic outflow of the cranial autonomic system On the median sagittal section of the brain the mesencephalon may be visualized as that portion between two lines of section the upper of which passes from the anterior margin of the superior colliculi to the posterior border of the mammillary bodies the lower of which passes from the inferior border of the quadrigeminal plate to the anterior border of the pons The upper of these sections when made in an experi mental animal produces decerebrate rigidity Such an animal is commonly known as a midbrain animal

Contrary to age old teaching the synaptic center for pupillary light reflex does not pass through the superior corpora quadrigemina but through a small area just anterior (ventral) to them (Fulton[4]) The center for pupillary con striction is the Edinger Westphal midline nucleus of the third nerve

The majority of the righting reflexes are integrated in the midbrain While the neck righting reflexes are integrated in the medulla and the optical in the cor

tex the labyrinthine righting reflexes body righting reflexes acting upon the head and body righting reflexes acting upon the body are integrated in the mesencephalon

There has been a great divergence of opinion concerning the function of the

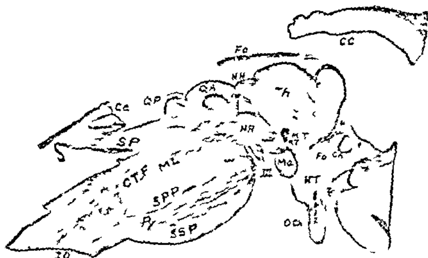


FIG 12 Author s drawing from myelin sheath section magnified The section is slightly parasagittal through the brain stem CC corpus callosum Fo fornix Ce cerebellum QP and QA posterior and anterior corpora quadrigemina NH habenular nucleus Th thalamus NR nucleus ruber SP superior cerebellar peduncle Ma mammillary body Ca anterior commissure CTF central tegmental fasciculus ML median lemniscus Py pyramidal tract SPP SSP stratum profundum and superficialis of the pons respectively OCh optic chiasm IO inferior olive

red nucleus in the mesencephalic righting reflexes (Fig 12) The discussion has centered around the question whether it was the red nucleus itself or neighboring structures through which the reflexes acted Magnus the great master in this field who received his inspiration from Sherrington has produced a remarkable monograph entitled *Korperstellung* dealing with the subject Rademaker wrote a good sized monograph called Die Bedeutung der roten Kerne und des ubrigen Mittelhirns fur Muskeltonus Korperstellung and Labyrinthreflexe in which the general region of the red nucleus was credited with much of this function

It seems that most of the difficulty in interpretation of physiology of the red

nucleus stems from anatomical difficulties It has been known for years that the inferior large celled portion of the red nucleus gives rise to the rubrospinal tract which crosses in Forel s decussation and descends into the spinal cord This tract however is a delicate bundle which has always seemed incapable of being the source of the large rubrospinal tract or of accounting for rubral influence on the anterior horn cells

On the other hand the much larger central tegmental fasciculus, which supposedly has had its origin from the thalamus has been shown by Spatz[10] to arise from the parvicellular portion of the red nucleus at the supero mesial angle It makes its way as a large compact bundle establishing relays with the tegmental reticular formation in the pons and medulla It sends fibers to the inferior olive and continues into the spinal cord in direct communication with the large ground bundle system This rubro spinal mechanism by its anatomical connections is peculiarly fitted to serve automatic extrapyramidal mechanisms

The large group of pigmented cells known as the substantia nigra is located ventral to the red nucleus and extends as a sheet in the cerebral peduncles Its connections are with the corpus striatum and with areas 4 and 6 of the cerebral cortex It is concerned with muscular tone but its exact physiological role is not determined It is the principal seat of inflammation in lethargic encephalitis

In the periaqueductal gray matter, in the superior portion of the mesencephalon and extending into the hypothalamus is a center concerned with sleep It may be looked upon as a structure which when active maintains attention and focuses consciousness and which when inactive permits sleep Its functional association with the diencephalon is so intimate that a sharp distinction is impossible Its further discussion is reserved for a consideration of the hypothalamus

Vegetative Nervous System

The vegetative nervous system is contained partly within the central nervous system where it is represented in the cortex thalamus hypothalamus mesencephalon, medulla and spinal cord partly in a paravertebral chain of ganglia with subsequent ramification in a series of plexuses in or about the viscera and finally, in fibers distributed with the peripheral nerves It is thus as extensive in its distribution as are the brain and spinal cord with all their peripheral nerves Fulton[4] defines the system although he calls it the autonomic nervous system, as " that part of the nervous system innervating smooth muscle cardiac muscle and the glands' In general the vegetative nervous system serves the function of maintaining homeostasis (Cannon)

The peripheral distribution of the fibers may be described as consisting of two parts harmoniously antagonistic (to use an accurate, although apparently para

Fig 13 Scheme of the vegetative nervous system (Modified from Grevin Handbuch der Neurologie Bumke Foerster Springer Berlin 1936)

dorsical term) the cranio sacral (greater vagal or parasympathetic) and the thoraco lumbar (or sympathetic) outflow (Fig 13) The antagonism may be illustrated by the action of the former in constricting the pupil slowing the heart and increasing bowel activity and the action of the latter in dilating the pupil, increasing the rate of the heart and reducing peristalsis Yet the actions of the two are coordinated beautifully to the ultimate benefit of the entire organism, any undue imbalance actually generating the clinical picture of illness The entire subject of psychosomatic medicine rests on improperly controlled balance in some division of this system

Both divisions of the vegetative nervous system are characteristized by origin within the central nervous system and occurrence of one synapse along every path thus one speaks of preganglionic and postganglionic fibers in every instance In the parasympathetic system the preganglionic fibers are relatively long and have their synapses close to or actually within the organ supplied They do not intimately reach the skin or body wall Their action is discrete they exert their force on certain organs (pupil salivary glands islands of Langerhans external genitalia bladder and rectum) and do not act en masse In the sympathetic system the synaptic junctions as a rule lie in ganglia of the prevertebral chain or in ganglia of prevertebral plexuses such as the coeliac and mesenteric plexuses Each preganglionic fiber contacts a large number of postganglionic fibers perhaps 20 or more in contrast to those of the other system in which they contact very few The sympathetic acts en masse, thus putting a large part of the body into instant readiness in an emergency

Speaking in general one may say that the parasympathetic system "presides" during peace i e over *anabolism* and hence is predominant during sleep The pupils then are relatively smaller blood pressure is lower heart rate slower blood sugar lower perspiration greater Emissions then occur and excretions are prepared The sympathetic system predominates during waking hours and hence during *catabolism* The body is keyed up for its contest with the outside world for fight or flight

The action of this portion of the system may be mimicked by injection of adrenalin the pupils dilate tachycardia appears blood pressure is elevated blood sugar rises gastric secretion is suppressed excretion of feces is suppressed also unless the whole organism is paralyzed with fear and all reproductive functions are abolished

The sympathetic division differs anatomically from the parasympathetic in having white rami communicantes through which the efferent motor fibers leave to enter the sympathetic chain of ganglia Through gray rami other fibers re enter the nerve to be distributed with it

Communicantes Vegetative Nervous System within the Spinal Cord

The cells of origin of the vegetative nervous system within the spinal cord are found in the lateral cornua of the gray matter The preganglionic fibers for the thoraco lumbar outflow (sympathetic) emerge from the first dorsal to the second lumbar segments inclusive They run in the anterior (motor) root until a point

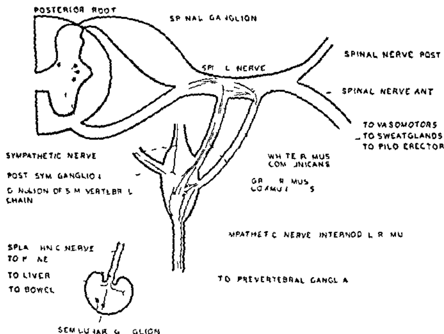


Fig 24 Scheme of the course of fibers in rami communicantes (Modified from Greving Handbuch der Neurologie Bumke Foerster Springer Berlin 1935)

is reached in the peripheral nerve beyond the gray ramus then flow out in the white rami communicantes to a synapse at the same level or higher or lower levels before a synapse is reached After a synapse the fiber reenters the nerve from the sympathetic chain through the gray ramus to be distributed with it In the cervical region there are no sympathetic emergent fibers tho e for the head emerge through the upper dorsal segments and ascend in the cervical sympathetic trunk There are usually three cervical ganglia and fibers continue upward from the superior cervical ganglion to be distributed through the (sympathetic) carotid nerves The dilator fibers for the pupil for instance arise in the hypothalamus pass downward through the entire brain stem and cervical cord to the

doxical term) the cranio sacral (greater vagal or parasympathetic) and the thoraco lumbar (or sympathetic) outflow (Fig 13) The antagonism may be illustrated by the action of the former in constricting the pupil slowing the heart and increasing bowel activity and the action of the latter in dilating the pupil, increasing the rate of the heart and reducing peristalsis Yet the actions of the two are coordinated beautifully to the ultimate benefit of the entire organism, any undue imbalance actually generating the clinical picture of illness The entire subject of psychosomatic medicine rests on improperly controlled balance in some division of this system

Both divisions of the vegetative nervous system are characteristized by origin within the central nervous system and occurrence of one synapse along every path thus one speaks of preganglionic and postganglionic fibers in every instance In the parasympathetic system the preganglionic fibers are relatively long and have their synapses close to or actually within the organ supplied They do not intimately reach the skin or body wall Their action is discrete they exert their force on certain organs (pupil, salivary glands islands of Langerhans external genitalia, bladder and rectum) and do not act en masse In the sympathetic system the synaptic junctions as a rule lie in ganglia of the prevertebral chain or in ganglia of prevertebral plexuses such as the coeliac and mesenteric plexuses Each preganglionic fiber contacts a large number of postganglionic fibers, perhaps 20 or more in contrast to those of the other system in which they contact very few The sympathetic acts en masse thus putting a large part of the body into instant readiness in an emergency

Speaking in general one may say that the parasympathetic system " presides " during peace i e over *anabolism* and hence is predominant during sleep The pupils then are relatively smaller blood pressure is lower heart rate slower blood sugar lower perspiration greater Emissions then occur and excretions are prepared The sympathetic system predominates during waking hours and hence during *catabolism* The body is keyed up for its contest with the outside world, for fight or flight

The action of this portion of the system may be mimicked by injection of adrenalin the pupils dilate tachycardia appears blood pressure is elevated blood sugar rises gastric secretion is suppressed excretion of feces is suppressed also unless the whole organism is paralyzed with fear and all reproductive functions are abolished

The sympathetic division differs anatomically from the parasympathetic in having white rami communicantes through which the efferent motor fibers leave to enter the sympathetic chain of ganglia Through gray rami other fibers re enter the nerve to be distributed with it

Vegetative Nervous System within the Medulla Oblongata

Vegetative centers within the medulla oblongata consist of the superior and inferior salivary nuclei and the dorsal vagus nuclei Through the vagus nerve fibers reach the heart bronchial tree and the gastrointestinal tract as far as the transverse colon Irritable carotid sinus is a syndrome sometimes resulting in epileptiform seizures Section of the ninth nerve at the medulla recently has relieved that condition

DIENCEPHALON
(Hypothalamus Thalamus Subthalamus)

The importance of the diencephalon and especially of the hypothalamus in the life of the individual is just coming to be fully recognized While without any cerebral cortex an individual (anencephalic monster) may exist breathe cry eat *and sleep without a hypothalamus he will die unless kept alive by artificial means* In the hypothalamus are integrated the highly organized visceral and somatic reaction patterns which are essential to life itself

Here it should be clarified that a decorticate animal (one deprived of its neocortex) as a result of the operation inevitably will lose more than the cortex for the simple reason that the thalami except for the mo t mesial portions will *degenerate A decorticate animal therefore* like an anencephalic monster is deprived of much of its diencephalon The portion of the diencephalon remaining is essentially the hypothalamus and subthalamus

Hypothalamus

Without any cerebral cortex an individual still shows emotions of a sort the sham rage of the decorticate animal or of the animal whose hypothalami are being stimulated by electrodes is classic Without hypothalamus there is no emotion One might state the matter differently and say that the hypothalamic patterns are the neuronal structures essential to emotion And inasmuch as all behavior is emotionally motivated it follows that the hypothalamus with the periaqueductal gray matter is the power house of the body it is the source of all dynamics Corroboration has come recently from the field of electroencephalography as Obrador[11] and Kennard[1] independently have shown that when the hypothalamus is destroyed all electrical activity of the cortex ceases

Masserman[13] has produced only *sham rage* by stimulation of the hypothalamus with fixed electrodes After the sham rage it was found conditioned reflexes which had been established before the stimulation were not lost This is evidence that the feeling tone was not aroused and on that basis Masserman

first and second dorsal segments then ascend through the sympathetic trunk to the superior cervical ganglion where the first synapse occurs (Figs 14 and 15) The fibers then ascend through the internal carotid nerves to where they can join the superior division of the trigeminal nerve to the orbit

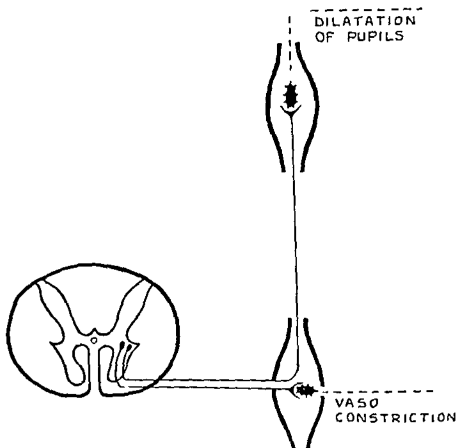


FIG 15 Course of preganglionic fibers as determined by the nicotine method (From Greving Handbuch der Neurologie Bumke Foerster Springer Berlin 1935)

The fibers for the sacral outflow arise from the lateral horns as do the sympathetic fibers and make their exit from the second to the fifth (sometimes only from the third and fourth) sacral segments They depart from the corresponding nerves and go in separate nerve bundles called the nervi erigentes and form their first synapses within ganglia of the pelvic plexuses or within the walls of the rectum or bladder

by the display The ability therefore of an experimenter to produce one component of emotion without the other does not prove that the engrams of emotion are not located in the area stimulated

Further evidence in the same direction is available in normal persons daily Many men are perfectly capable of strong sex desire and even gratification as a purely mechanical act without any material component of feeling tone Instances are numerous of men after paying a prostitute for sexual satisfaction for a long period of time finally falling in love with the woman i e developing a feeling tone which then completes the emotion All of the well known love making of the stage and screen depends on the ability of the player to go through the act without having the feeling tone

Much evidence has appeared to show that the hypothalamus is also the seat of the patterns constituting personality Human infants show personality at birth yet the brain is not myelinated above the diencephalon in any association areas Litter puppies and kittens at birth show personality differences and inasmuch as the cerebral cortex is a blank state with association tracts unmyelinated and with no records of any experience at the time of birth the engrams of personality must reside below the cortex Hypothalamic lesions of lethargic encephalitis notoriously cause changes of personality Neoplasms affecting the walls of the third ventricle almost regularly cause personality changes Psychiatrists find that the constitutional psychopathic personality is almost entirely refractory to alteration because personality depends on congenital reaction patterns not on cortical patterns which are the result of training and subject to intellectual control (see The Hypothalamus Assoc Research Nerv and Ment Dis 1939 especially the paper by Alpers[15])

The hypothalamus with the anterior part of the mesencephalon is the center of consciousness when the hypothalamus is out of function the individual is in coma regardless of intactness of the entire cortex In the metaphor used above in which the hypothalamus was called the power house of the body the simile is apt that when the power is off the factory cannot function even though the entire office staff is present If an intermediate connection is broken as when the thalamus is out of function bilaterally the result is almost the same so far as capacity for function is concerned Stern[1] has reported a case with bilateral degeneration of the thalamus as the only lesion The patient first showed hypersomnia then progressive dementia and finally coma Many clinical cases have now made clear that lesions in the thalamus cause a profound *disturbance of attention* and attention is the focus of consciousness

As the diencephalon is the seat of the emotions it follows that as stated it is the seat of motivation It is therefore the seat of *purpose* in life it is the basis of all instinctive drive all behavior

concludes that sham rage is not true emotion Since only sham rage is elicited by hypothalamic stimulation and not the appropriate feeling tone, Masserman concludes that the hypothalamus is not the seat of the emotions

There are several important objections to such conclusions In the first place only a small portion of the hypothalamus was thus stimulated and that portion was not the same as that stimulated by Foerster traction on the hypothalamic floor did result in arousing of feeling tone In the second place, it evidently makes quite a difference whether the impulses are started from an electrode or by simple traction or by rubbing It is to be recalled that sponging of the anterior floor of the third ventricle caused sexual pleasure in one of Foerster s patients while in another compression of the posterior part by a tumor caused emotional depression But in that location rubbing or traction did not give the symptom only compression did so Further, feeling tone is not the only element of emotion all the appropriate vegetative reactions help to make up the whole pattern and the presence of the intact cortex greatly elaborates it

As is usual, when emotions of investigators are aroused in scientific discussions about interpretation of observations, the difficulty lies in the lack of exact definitions What is emotion? Masserman regards emotion as feeling tone He considers sham rage devoid of emotion because the feeling tone either ceases immediately when the stimulus producing the sham rage is removed or because there is no feeling tone at all His principle seems to be that feeling tone cannot cease suddenly Yet it is common experience that certain types of persons fly into a rage and become calm instantly upon removal of the stimulus which causes the emotion It is also common experience to see persons of another type who cannot become calm for days The duration of the feeling tone should therefore not be a criterion to determine whether or not emotion is present Emotion is far more than feeling tone it embodies consciousness of it in most instances and also memory of it plus all of the visceral and somatic manifestations of it

What seems to the writer crucial evidence that the engrams of emotion are located basically in the diencephalon consists of two facts (1) the human infant shows emotion at birth yet there is no myelination of any of the association fiber systems of the brain (2) the normal infant at birth does not have electroencephalographic waves except irregular show waves with a frequency of one half to two per second (Berger Davis and others see Gibbs and Gibbs[14])

Dissociation of the vegetative reaction from feeling tone is well known clinically In a case of parkinsonism with pseudobulbar palsy observed by the writer the patient showed marked involuntary crying When asked whether he had the appropriate tone the patient replied Goodness no! When I get to crying I look in the mirror and laugh at myself crying Patients with pseudobulbar palsy also may start laughing and be unable to cease even though they are embarrassed

by the display The ability therefore of an experimenter to produce one component of emotion without the other does not prove that the engrams of emotion are not located in the area stimulated

Further evidence in the same direction is available in normal persons daily Many men are perfectly capable of strong sex desire and even gratification as a purely mechanical act without any material component of feeling tone Instances are numerous of men after paying a prostitute for sexual satisfaction for a long period of time finally falling in love with the woman i e developing a feeling tone which then completes the emotion All of the well known love making of the stage and screen depends on the ability of the player to go through the act without having the feeling tone

Much evidence has appeared to show that the hypothalamus is also the seat of the patterns constituting personality Human infants show personality at birth yet the brain is not myelinated above the diencephalon in any association areas Litter puppies and kittens at birth show personality differences and inasmuch as the cerebral cortex is a blank state with association tracts unmyelinated and with no records of any experience at the time of birth the engrams of personality must reside below the cortex Hypothalamic lesions of lethargic encephalitis notoriously cause changes of personality Neoplasms affecting the walls of the third ventricle almost regularly cause personality changes Psychiatrists find that the constitutional psychopathic personality is almost entirely refractory to alteration because personality depends on congenital reaction patterns not on cortical patterns which are the result of training and subject to intellectual control (see The Hypothalamus Assoc Research Nerv and Ment Dis 1939 especially the paper by Alpers[15])

The hypothalamus with the anterior part of the mesencephalon is the center of consciousness when the hypothalamus is out of function the individual is in coma regardless of intactness of the entire cortex In the metaphor used above in which the hypothalamus was called the power house of the body the simile is apt that when the power is off the factory cannot function even though the entire office staff is present If an intermediate connection is broken as when the thalamus is out of function bilaterally the result is almost the same so far as capacity for function is concerned Stern[16] has reported a case with bilateral degeneration of the thalamus as the only lesion The patient first showed hypersomnia then progressive dementia and finally coma Many clinical cases have now made clear that lesions in the thalamus cause a profound *disturbance of attention* and attention is the focus of consciousness

As the diencephalon is the seat of the emotions it follows that as stated it is the seat of motivation It is therefore the seat of *purpose* in life it is the basis of all instinctive drive all behavior

Coming down to the physiological functions, which underlie behavior, we find the hypothalamus to be the fundamental regulator of visceral and somatic physiological correlation Its presence is essential to the maintenance of blood pressure, pulse rate respiration rate body temperature It regulates blood sugar, fat and carbohydrate metabolism in general and some constituents of the blood chemistry As it largely governs the pituitary gland it largely controls the entire endocrine system it regulates sex function and libido, growth the metabolic rate, hunger and thirst water metabolism in a measure the blood cell level and the orderly function of the gastrointestinal tract One might generalize and say that it governs by virtue of its being the seat of the primary neurons of it, the entire sympathetic nervous system

While the sympathetic neuronal patterns are in general more scattered than the parasympathetic ones the posterior nuclei are more concerned with the former, and the middle and anterior more with the latter

It is true that there are cortical areas which by stimulation have been shown to exert influence on vegetative functions but this influence is of minor importance the hypothalamus is the center of the system and while the cortical level is in a sense above it it is of only secondary value to the body in the function of visceral regulation

Foerster[16] and later others have shown that irritation of the anterior portion of the floor of the third ventricle causes hypomanic activity with disturbance of judgment ribald laughter etc all of which ceases when the irritation is removed (see paper by Alpers[1]) Pressure of tumors on the posterior portion produces moroseness and dullness In the posterior portion adjacent to the mesencephalon lesions produce sleep and stupor going on to coma Here we may correlate the fact that the anterior patterns are more concerned with parasympathetic function, left intact in such lesions and predominate during sleep while the sympathetic functions, destroyed by such lesions are largely submerged during sleep

From anterior and midline nuclei in the region of the tuber cinereum there are evoked bladder contractions cardiac inhibition increased peristalsis of the stomach and bowel and sweating to control body temperature Blood sugar also is regulated here and destruction of the supraoptic nuclei causes diabetes insipidus Occasionally lesions in this area upset body chemistry to cause diabetes mellitus without ketosis and may give the symptoms of urinary retention, thus simulating uremia Even fat metabolism may be disturbed by lesions of the hypothalamus leading to obesity or cachexia

Cooling of the hypothalamus causes pilo erection and shivering while heating may result in sweating or hyperthermia Traumatic lesions may cause the latter also

The clinical syndromes which may be evoked from the hypothalamus either

by irritation or destruction have been listed by Riddoch as follows (1) diabetes insipidus, (2) bulimia (3) glycosuria with or without hyperglycemia (4) obesity and cachexia (5) sexual disorders amenorrhea impotence, loss of or increase of libido adipo ogenital syndrome (6) sleep disorders including narcolepsy (7) thermal dysregulation, (8) polycythemia or leukocytosis (9) ulceration of the upper alimentary tract (10) autonomic diencephalic epilepsy and (11) emotional disorders

With the development of the cerebral cortex fiber connections have been established with the diencephalic centers The cortical centers for autonomic regulation are located close to the somatic centers for the same functions Thus cardiovascular reactions have been obtained from Brodmann areas 4 and 6 obviously to stimulate vegetative responses to motor activity In such situations both sympathetic and parasympathetic centers are located together as both vasoconstriction and vasodilation can be obtained by electrical stimulation of areas 4 and 6 The frontal region also is capable of influence on peristaltic function a necessary relaxation for volitional influence on eliminative function

Thalamus

Within the last decade the thalamus has been studied repeatedly and intensively by a number of men including Clark[1] Papez and Walker [1] and a considerable reorientation has resulted A combined anatomophysiological summary may be given as follows The anteroventral nucleus (Walker s terminology) receives fibers from the mammillo thalamic tract and projects to the cingulate gyrus and to the paracentral lobule From the cingulate gyrus fibers go to the orbital cortex

The dorso median nucleus is a relatively large mass bluntly pointed anteriorly swelling to a considerable width in the central portion and bifurcated posteriorly where it appears on both sides lateral to the habenular nuclei The me ial portion is magnocellular the dorsolateral is parvocellular The large-celled portion seems to be the connecting link between the periventricular gray matter of the hypothalamus and the orbital portion of the frontal lobes Here then is the thalamic portion of the engram system of personality The small celled part projects to areas 9 10 and 12 of Brodmann The lateral posterior nucleus is linked similarly but the parietal cortex is the portion with which connections are made The centromedian nucleus is connected closely with these nuclei in the thalamus but it does not project to the cortex

The large anteriorly placed ventrolateral nucelus receives the fibers of the brachium conjunctivum (superior cerebellar peduncle) direct from the dentate nucleus and projects to areas 4 and 6 of Brodmann It is through this connec ti n that the cerebellum regulates motor cortical functions

The large posteroventral nucleus and the arcuate nucleus are organized alike The latter serves for the facial and laryngeal areas including the organs of taste and the trigeminal area The former serves for the body below the face the spinothalamic tract terminates behind the site for the median lemniscus This nucleus projects to the postcentral convolution lesions between it and the cortex cause only hypesthesia lesions within the thalamus may cause anesthesia and central pain

The posterior portion of the thalamus includes the pulvinar and the geniculate bodies The lateral geniculate is a way station for vision a lesion of it causes homonymous hemianopia The median geniculate body serves similarly for hearing but as fibers from both cochlear ganglia project equally to both median geniculates a lesion of one does not cause deafness in either ear

Subthalamus

The region known as the subthalamus is bounded superiorly by the thalamus anteriorly by the hypothalamus with which it merges imperceptibly inferiorly by the mesencephalon and laterally by the cerebral peduncle as it ascends to become the internal capsule It contains the corpus subthalamicum of Luys part of the substantia nigra part of the zona incerta and many fiber tracts The body of Luys is important because a lesion in it gives rise to hemiballismus of the opposite upper limb The mesial portion of the subthalamus is somehow concerned with retention of basic consciousness because hemorrhage into it bilaterally or severe inflammatory reaction produces coma

Corpus Striatum

The corpus striatum consists of the caudate nucleus and the lenticular nucleus The latter consists of the putamen and the globus pallidus The chief connections are with the thalamus the body of Luys and the substantia nigra The physiology is imperfectly known yet it is clear from clinico pathological and phylogenetic studies that the corpus striatum has an enormous influence on the physiology of the general motor mechanism

The cerebral cortex is a recent phylogenetic acquisition yet lower vertebrate forms without any material quantity of cortex have adequate motor function for their purposes Myelogenetic studies classically those of Flechsig show that in the new born infant the corpus striatum is fully myelinated while the pyramidal tract is not developed to functional capacity It is generally believed that the human intrauterine motor activity is mediated by the extrapyramidal system and it seems evident from observation of the normal infant during the first few months

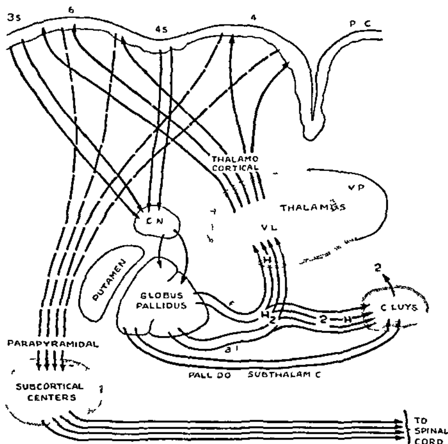


Fig 16 Bucy's scheme to illustrate the cortical basal ganglionic functional interrelationships (Redrawn from Bucy The Precentral Motor Cortex Univ Ills Press Urbana 1944)

of the life that the gradual withdrawal of extrapyramidal control in favor of pyramidal occurs as the new system becomes myelinated

There is also an experimental approach to the problem Dr Kennard[1] has decorticated monkeys both old and young and she has severed the pyramids at the medulla in both old and young While the older animals have great difficulty in *adjusting to such violent subtractions from their motor mechanisms* the young ones do surprisingly well It is evident that extrapyramidal mechanisms are adequate to permit purposeful movements

Dr Sarah Tower (Bucy [7]) has done similar and also additional independent

work Notably she has sectioned the pyramids without producing complete paralysis of voluntary movement Her conclusions are that stereotyped movements generally are initiated by the extrapyramidal system

In harmony with these phylogenetic, ontogenetic and experimental studies are the findings on human material by such men as Jakob , Wilson[33], the Vogts, Bonhoeffer and others studying clinico pathological cases In the former group of studies the material consisted chiefly of cases of cortical absence or deficit in the latter group the opposite approach is taken by the study of destruction or deficit of the corpus striatum The classical paralysis agitans throws a great deal of light on the subject

Patients with paralysis agitans suffer chiefly with degeneration of the projection fiber system of the globus pallidus Now, that system does not project directly to the spinal cord but instead to the thalamus and the corpus subthalamicum of Luys then back to the inhibitory areas of the motor cortex Yet the effect of degeneration is manifest in the types of movements of which the patients are capable or incapable The abnormalities may be studied in two groups of disturbances tonic and phasic

Bucy[1] has worked out a system which explains the tonic phase of disease of the corpus striatum (Fig 16) He invokes the recently discovered suppressor strips of cerebral cortex notably the ones known as 4S between areas 4 and 6 and 8S anterior to area 6 of Brodmann These areas have, by stimulation, a suppressor effect on areas 4 and 6 which in turn have connections with the anterior horn cells through undetermined subcortical centers

By an elaborate anatomical and physiological analysis of the known mechanisms Bucy explains choreoathetosis and tremor the disturbances of the tonic phase of the ganglionic disease In brief he considers the abnormal movements to be the result of removal of inhibition of the frontal extrapyramidal cortical areas

For an explanation of the phasic disturbances of paralysis agitans and more or less similar diseases of the basal ganglia we are indebted to the studies of Jakob, Wilson and others and the corroborative experimental evidence of Kennard and Tower

To review the first, the clinical evidence of the phasic manifestations, from cases of marked paralysis agitans I wish to present the following

The patient loses his ability to perform *habitual acts* and to make *habitual movements* Above all he loses power to *initiate acts* and *movements* There is difficulty in *planning an act* because he has lost one of his mechanisms He cannot *start to walk*, and when once started, he cannot walk normally he shuffles his feet If he wishes to turn over in bed, he cannot ' figure out ' how to do so He cannot initiate the movements of feeding himself of rising from his chair or

of taking a step If once started walking he cannot initiate a change, he cannot stop Hence the propulsion and retropulsion

He has lost his *automatic association movement patterns* He does not swing his arms in walking, does not put his feet close to the seat nor support his weight by placing his hands on the chair on rising does not throw his head back to look directly up etc He has to give thought to all these movements and acts

His posture also is peculiar in that it is dependent on weakness of the anti gravity muscles There is characteristically a long sweeping kyphosis of the upper dorsal spine and a tendency to flexion of the knees and elbows The mouth tends to drop open The finger postures are not so clearly related to weakness of antigravity muscles the phalangeal joints are extended the metacarpo phalangeal joints flexed the thumb extended It is tempting to assume that the extrapyramidal system innervates the red musculature but as all systems use the final common motor pathway such a selectivity is unlikely although not impossible Certain anterior horn cells might send their axons to the red while others send theirs to the white muscles It is still true that the *habitual contraction* of the antigravity muscles suffers in paralysis agitans

With all this obvious difficulty in the performance of habitual acts the patient with paralysis agitans can do the *unusual* He can catch a ball about as well as he could before his illness appeared he can run much better than he can walk he can walk with an artificial gait such as a high steppage gait or with steps unusually long Inasmuch as the cortical patterns are then used he does not imitate his usual gait well he caricatures One of my patients who played the piano daily but the violin only rarely was afflicted with paralysis agitans I had her try the violin when she could no longer play the piano To her surprise she could finger the strings very well

In all of this exposition one sees clearly that *habitual movements* and *acts* are not performed well in cases of disease of the basal ganglia but rare movements for which the cortex and the element of attention are used are well performed It was this generalization which led Jakob to believe that as acts became habitual they are relegated to the patterns in the basal ganglia The situation seems to be the following In earliest infancy the individual performs his acts crudely and only with the extrapyramidal system As the pyramidal system becomes functionally active it is used not to initiate the movement (initiation remains with the extrapyramidal system) but to control it in the interests of doing new things requiring dexterity and accuracy As soon as dexterity and accuracy have been attained the attention no longer is necessary and when that point is reached the pyramidal tract is no longer necessary for that act However if the act is to be modified or improved the pyramidal tract is again called into use by means of the attention When any movement or act becomes habitual the attention is no

longer required the pyramidal tract is little used if at all, the act fatigues one very little, and it appears to be relegated to the extrapyramidal system However, it is not really relegated it is merely left to itself without supervision of the pyramidal system

The extrapyramidal (striatal system) has one other function, which should be stated namely inhibition of tone of skeletal muscles In cases of section of the extrapyramidal tract the deep reflexes are increased This is in contrast to the effect on the deep reflexes of section of the pyramidal tract, which operation diminishes the tone These facts have come to light through the work of Sarah Tower

PALLIUM

The pallium is defined as the cerebral cortex with its subjacent white matter The cortex itself only a few millimeters thick is not entirely uniform even on gross inspection The extent of the primary visual cortex can be discerned with the naked eye because of the stripe of Gennari which is essentially a union of two bands of Baillarger These white bands are simply zones in which association axons are located in layers If the cortex is stained for cell bodies and examined under moderate magnification it is seen that layers of cells are discernible, although the demarcation is not sharp in all instances The importance of these facts lies in their physiological implications the cortex is an organized layer of neurons with innumerable interlacing patterns and complexity of neuronal connections baffling imagination Adjacent gyri are associated by means of short fiber systems the U fibers and more distant ones by means of fibers of appropriate length The entire white matter consists of fibers which take their origin in the cortex except relatively few projection fibers arising from nuclear masses below

On the basis of cellular arrangement of the neurons in the cortex cytoarchitectonic studies, and without any reference to physiology the entire cortex has been mapped out into areas (Fig 17) This was done first by Brodmann later much more in detail by Economo and Koskinas [4] also by the Vogts and by Campbell Bailey and von Bonin and others recently have made new contributions These cytoarchitectonic areas are not sharply delimited in every instance several observers working simultaneously do not agree upon the exact line of transition from one to the next On reflection one would expect such gradation because each must be able to associate with its neighbor and therefore must merge

Sulci and gyri do not by any means always constitute the borders of cytoarchitectonic areas for which reason one cannot simply place numbers on the gyri A separate map must of necessity be made one in which the gyri are indicated merely for convenience of anatomical correlation The central sulcus does

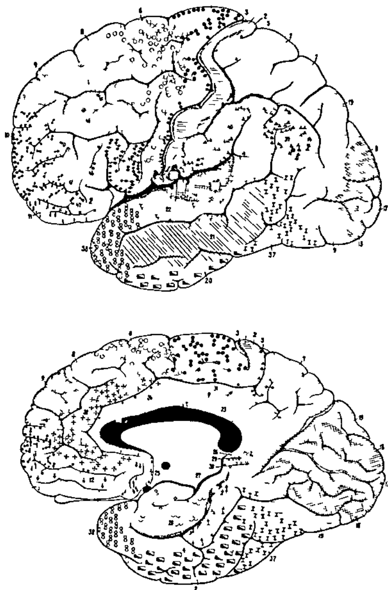


FIG 17 Brodmann's cytoarchitectonic cortical areas

separate areas, but the calcarine fissure does not, although they are both primary fissures

The great master of neurology, Hughlings Jackson [6] postulated many important neurological principles in the realm of physiology and also of clinical neurology which have been verified since then. He understood thoroughly the principles of division of labor in the cortex particularly as related to motor function. Dusser de Barenne, Fulton, and many workers at the Yale University physiological laboratory have established by the physiological method certain interrelations between cytoarchitectonic areas which have not been shown clearly anatomically. Thus a certain area may "fire" another at some distance, while the charge does not function in the opposite direction.

The Vogts, Dusser de Barenne, Tower, and others have shown in experimental animals that certain narrow strips of cerebral cortex respond to electrical stimulation only by inhibiting other areas. Garol and Bucy [7] recently have observed the same fact in the human subject. Whether or not these suppressor strips can be shown to have a distinctive cytoarchitectural appearance does not seem a matter of great importance; identical arrangement of cell layers might easily permit different neuronal connections in such a way as to produce inhibition instead of stimulation. Thus we are confronted with the necessity of admitting that apparent identity of cytoarchitectonic structure does not preclude difference in clinical physiological function. Certain areas certainly have functions not related to perception or to motor activity, inasmuch as much of the cortex is utilized for planning, thinking in general, for formation of ideas and for judgment. And much of our information still is fragmentary. For these reasons it is still impossible to list each cytoarchitectonic area with its corresponding physiology, deficit syndrome and effect of stimulation. The available knowledge is outlined below.

Occipital Lobe

All of the occipital lobe is devoted to vision, visual associations and visual memory. There are three distinct spheres of activity, area 17, area 18 and area 19 of Brodmann.

Area 17, area striata (borders of the calcarine fissure) serves for *primary visual perception* (Fig. 18). Irritation causes flashes of light to appear; destruction bilaterally causes blindness.

Area 18, area parastriata, serves for *recognition of visual images*. On the basis of clinical pathological material it is believed that the superior portion is more concerned with animate, the inferior with inanimate objects. Irritation of area 18 by the electrical current produces an image of a light standing still in the opposite visual field. It also causes the eyes to deviate away from the side

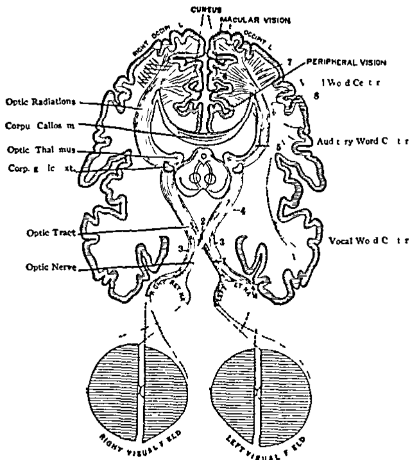


Fig 18 —Diagram of Visual Paths (Modified from Vialet)

Lesion at	1	produces Blindness of one eye
	2	Bi temporal hemianopia
	3 and 3	Bi nasal hemianopia
	4	R hemianopia with hemiopic pupil reaction
	5	normal pupil reaction
	6	
	7	Loss of visual orientation and localization in space
	8	Word blindness.

(C i y f Edw J A old P bl h)

Fig 18 Diagram of visual paths (From Purves Stewart Chapt I Vol. vi Oxford Medicine Oxford Univ Press New York 1926)

stimulated Destruction (bilaterally) renders the patient unable to recognize any object seen causes visual agnosia for objects

Area 19 area peristriata, serves for *revisualization of images* As for area 18, in area 19 there seems to be a division of function, the superior portion serving especially for animate the inferior especially for inanimate objects Irritation causes visual hallucinations in the opposite half fields destruction loss of power of visual reminiscence in the visual sphere The patient may have autotopagnosia, complete or partial or may visualize animate objects including his own body, while failing to revisualize his home streets and geography in general

Temporal Lobe

The neopallial temporal cortex is devoted to hearing and to auditory associations in general These include sounds in general music and spoken language The farther one withdraws downward and backward from Wernicke s area, the more *interpretation* is involved

Area 52 of Brodmann the transverse temporal gyri serves for auditory perception Results of irritation are not directly known because the area is inaccessible to stimulation Destruction causes total deafness Unilateral destruction causes no appreciable loss of hearing because both areas receive fibers from both ears

Areas 41 and 42 (functional distinction is not possible) area of Wernicke, serve for *recognition of sounds except musical ones* Irritation (Foerster[10]) causes hallucinations of hearing voices Destruction causes total lack of recognition of sounds auditory agnosia Unilateral destruction causes auditory agnosia word deafness only if the major side is destroyed

Area 38 anterior portion of the superior temporal convolution serves for *recognition of musical sounds* Irritation in some clinical cases has caused musical hallucinations results of electrical stimulation are not known Bilateral destruction causes musical deafness Unilateral destruction is soon recovered from

Areas 20 21 and 22 serve for interpretation and recall of auditory impressions Irritation causes auditory hallucinations destruction causes incomprehension of spoken language

The uncinate gyrus and the temporal paleocortex in general are concerned with olfactory perception recognition and recall functional distinction between the various areas is not possible Irritation causes olfactory hallucinations It may be said that the uncinate gyrus is far more definitely concerned with smell than is the cingulate gyrus pericallosal cortex

Area 37 posterior portion of the temporal cortex is devoted to formulation of language (Nielsen [9]) irritation has not produced recognizable symptoms but

destruction of the major side or of both sides cau es inability to marshal one s words to form sentences One cannot recall names of objects

Parietal Lobe

The parietal lobe except the supramarginal and angular gyri is concerned with general ensory perception recognition and interpretation It is divided into three portions the postcentral gyrus and the superior and the inferior parietal lobules The inferior lobule consists of the supramarginal (area 40) and angular (area 39) gyri the latter of which has a highly specialized function entirely different from that of the remainder of the parietal lobe (Nielsen)

Areas 1 and postcentral gyrus serve for primary perception of general sensation Irritation causes contralateral paresthesias of numbness and tingling Destruction causes hypesthesia and astereognosis By virtue of its connections with the precentral gyrus irritation also causes Jacksonian seizures

Area 5 of Brodmann is not clearly unde stood Its function seems related to the posture of the opposite lower limb inasmuch as stimulation causes flexion instead of extension of the contralateral lower limb

Area 7 superior parietal lobule is concerned with elaboration of general sensory impressions localization recognition and interpretation Irritation causes contralateral paresthesias of numbness and tingling Destruction cau es hyperesthesia and astereognosis The functional distinction between this area and the postcentral gyrus apparently is one of degree lesions cause more disturbance in the postcentral gyrus than in the superior parietal lobule

Area 39 angular gyrus is devoted to recognition and recall of visual images of letters mathematical figures musical notes syllables and words Results of irritation are unknown destruction of the major side or of both sides causes visual verbal and musical agnosia alexia and by virtue of loss of revisualization of the symbols also agraphia

Area 40 supramarginal gyrus is not entirely understood Its cortex seems to form a special correlation center for planning of motor acts upon the reception of the necessary sensory impressions Results of irritation are not known but acute destruction causes apraxia When progression of the lesion ceases the apraxia disappears Even bilateral destruction does not cause lasting apraxia This gyrus seems to form an important part of the posterior association area of Flechsig

Frontal Lobe

The frontal lobes are among the last to have become even fairly well under stood The precentral gyrus and the speech area have been pretty well compre

stimulated Destruction (bilaterally) renders the patient unable to recognize any object seen causes visual agnosia for objects

Area 19 area peristriata, serves for *revisualization of images* As for area 18, in area 19 there seems to be a division of function, the superior portion serving especially for animate the inferior especially for inanimate objects Irritation causes visual hallucinations in the opposite half fields destruction, loss of power of visual reminiscence in the visual sphere The patient may have autotopagnosia, complete or partial or may visualize animate objects including his own body, while failing to revisualize his home streets and geography in general

Temporal Lobe

The neopallial temporal cortex is devoted to hearing and to auditory associations in general These include sounds in general music and spoken language The farther one withdraws downward and backward from Wernicke s area, the more *interpretation* is involved

Area 52 of Brodmann the transverse temporal gyri serves for auditory perception Results of irritation are not directly known, because the area is inaccessible to stimulation Destruction causes total deafness Unilateral destruction causes no appreciable loss of hearing because both areas receive fibers from both ears

Areas 41 and 42 (functional distinction is not possible) area of Wernicke serve for *recognition of sounds except musical ones* Irritation (Foerster[16]) causes hallucinations of hearing voices Destruction causes total lack of recognition of sounds auditory agnosia Unilateral destruction causes auditory agnosia word deafness only if the major side is destroyed

Area 38 anterior portion of the superior temporal convolution, serves for *recognition of musical sounds* Irritation in some clinical cases has caused musical hallucinations results of electrical stimulation are not known Bilateral destruction causes musical deafness Unilateral destruction is soon recovered from

Areas 20 21 and 22 serve for interpretation and recall of auditory impressions Irritation causes auditory hallucinations destruction causes incomprehension of spoken language

The uncinate gyrus and the temporal paleocortex in general are concerned with olfactory perception recognition and recall functional distinction between the various areas is not possible Irritation causes olfactory hallucinations It may be said that the uncinate gyrus is far more definitely concerned with smell than is the cingulate gyrus pericallosal cortex

Area 37 posterior portion of the temporal cortex is devoted to formulation of language (Nielsen[9]) irritation has not produced recognizable symptoms but

engrams for patterns of swallowing and chewing a unilateral lesion of the major side only causes dysphagia an apraxia of swallowing There is some evidence for the concept that the cortical sense of taste is located here but I am skeptical and Bailey[31] whose opinion based on cytoarchitectonic grounds is valuable does not accept the idea

Area 44 Broca s convolution is the seat of engrams of memory of how to move the vocal organs for purposes of speech Stimulation causes repetitive speech

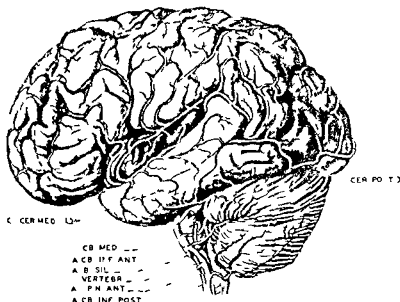


Fig 19 Gross circulation of cerebrum and cerebellum lateral view

without the will of the patient and destruction of the major side only or of both sides causes mutism until the other side is trained (Henschen also Nielsen)

Area 45 pars triangularis of the third frontal convolution contains engrams of the patterns of motor musical function both vocal and instrumental Musical production by electrical stimulation has not been evoked but ablation causes avocalia

The portion of the frontal lobe anterior to area 8 superiorly and to area 45 inferiorly comprises areas 9 10 11 12 32 46 and 47 and especially the orbital cortex and is concerned in a large measure with *consciousness of self* and with

hended for some time but only within the last quinquennium have the 'premotor" and ' prefrontal portions come within the bounds of comprehension In general the premotor portion of the frontal lobes is not concerned with formation of concepts concepts are formed so completely in the posterior association area of Flechsig that both premotor areas may be ablated without loss of any memories On the other hand the anterior portion of the frontal lobes through their intimate connections with the diencephalon are of primary importance in wisdom They utilize the concepts tored as engrams in the posterior portion of the brain, decide on the basis of past experience what is best for the future and thus modify, so far as modification is possible the personality of the individual

Area 4 area gigantopyramidalis constitutes a portion of the precentral gyrus It is wide on the mesial surface and diminishes in width to almost zero near the sylvian fissure This cortical area gives rise to a large part of the pyramidal tract, but the pyramids are not made up entirely of fibers from area 4 This tract is not the only source of corticospinal motor fibers, at any rate, because, after ablation of area 4 electrical stimulation of area 6 still provokes massive turning movements of the contralateral side of the body The function of the fibers from area 4 is to perform accurate and fine (discrete) voluntary movements Electrical stimulation provokes focal movements and if electrodes of sufficiently small size are utilized, even the contractions of individual muscles such as an interosseous of the hand are obtained One of Hughlings Jackson's greatest contributions to neurology was his analysis of the progression of movements down or up the body musculature upon irritation of the motor cortex

Tower[17] recently has shown that the pyramidal tract has a tonic effect on the deep reflexes its destruction diminishes them as already elucidated in an earlier portion of this chapter

Area 4S was not delineated by Brodmann but has been demonstrated physiologically by Tower, by Dusser de Barenne and McCulloch[30] and others in animals and by Garol and Bucy [7] in man It forms a narrow strip between areas 4 and 6 Electrical stimulation causes suppression of a voluntary movement already started Destruction causes marked spasticity

Area 6 of Brodmann prepyramidal motor cortex causes upon electrical stimulation massive turning movements of the body toward the opposite side The signs of its destruction in a normal person are not clear in a patient with contralateral choreoathetosia its ablation tends to prevent the movements

Area 8 of Brodmann located anterior to area 6S seems not to have a uniform physiology Its lower end contains engrams for movements in writing and for turning of the head and eyes The remainder is insufficiently understood, but Bucy has shown that it has a suppressor effect on voluntary movements

Area 43 of Brodmann the pararolandic opercular area, certainly contains

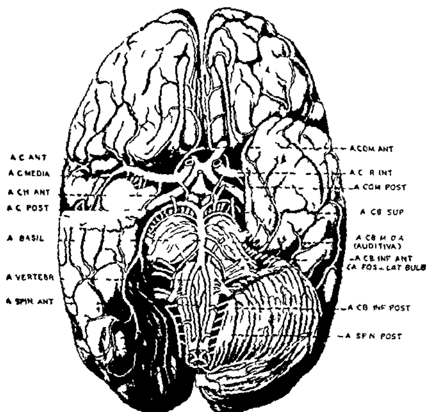


Fig 21 Gro s circulati n of cerebrum and cerebellum basilar view The tip of the right temporal lobe has been removed to display some of the deeper branches of the m ddle cerebral artery

the posterior cerebral arteries These are shown in the illustrations (Figs 19 to 21)

By means of the two posterior communicating arteries between the internal carotids and posterior cerebrals and through the anterior communicating artery between the two anterior cerebrals the circle of Willis is formed

As shown in the illu trations (Figs 19 20 and 21) the middle cerebral arteries supply the entire lateral portion of the cortex as well as the corpus striatum except for a margin in the uperior anterior one half which is supplied by the anterior

judgment This analysis was stressed by Kleist[34] in his study of war injuries of World War I and the same theme is discernible in Brickner's[35] analysis of his case of bilateral prefrontal lobectomy It comes to the fore in striking degree in Freeman and Watts analysis of their more than 200 cases of prefrontal lobotomy

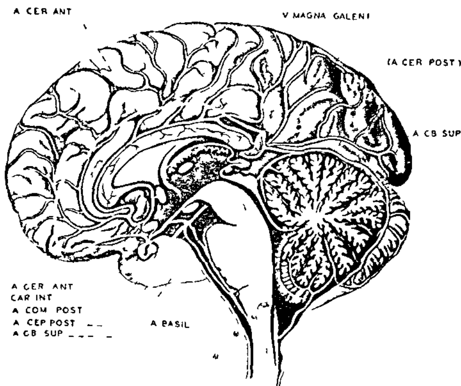


FIG 20 Gross circulation of cerebrum and cerebellum mesial view

CIRCULATION OF THE BRAIN

The cerebrum is supplied by blood almost entirely through the internal carotid and the posterior cerebral arteries The internal carotid arteries give off the anterior cerebrals and continue as the middle cerebral arteries running up into the sylvian fissure The two vertebral arteries unite to form the basilar artery, which lies along the anterior surface of the pons The basilar divides into two to form

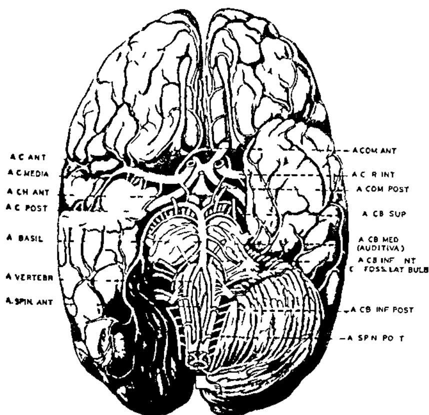


FIG 21 Gross circulation of cerebrum and cerebellum ba ilar view The tip of the right temporal lobe has been removed to di play some of the deeper branches of the middle cerebral artery

the posterior cerebral arteries These are shown in the illustrations (Figs 19 to 21)

By means of the two posterior communicating arteries between the internal carotids and po terior cerebrals and through the anterior communicating artery between the two anterior cerebrals the circle of Willis is formed

As shown in the illustrations (Figs 19 20 and 21) the middle cerebral arteries supply the entire lateral portion of the cortex as well as the corpus striatum except for a margin in the superior anterior one half which is supplied by the anterior

cerebrals, and a similar margin in the posterior and inferior portions, which is supplied by the posterior cerebral arteries The mesial surface of the hemispheres is supplied entirely by the anterior and posterior cerebral arteries The inferior surface of the temporal lobe and nearly all of the occipital lobes receive their blood supply from the posterior cerebral arteries The brain stem and cerebellum (surfaces and interior) receive their supply through branches of the basilar and posterior cerebral arteries

The anterior choroidal artery is a fairly large branch of the middle cerebral artery which turns backward to supply much of the choroid plexus of the lateral ventricle Its importance lies in the fact that it also supplies part of the thalamus and the posterior portion of the internal capsule A lesion of it causes a focus of softening illustrated at 5 in Fig 18

The general rule applies that the surface arteries, unless they are the seat of aneurysms or unless they are traumatized hardly ever rupture On the other hand they are subject to thrombosis The arteries which receive part of their support from the brain substance are the ones which commonly rupture

The surface venous drainage of the cerebrum takes place in two directions, upward to the superior sagittal sinus and downward to the lateral and sigmoid sinuses The deep drainage from the ventricles is through the deep cerebral veins, vein of Galen and straight sinus to the torcular The lateral ventricles are drained by means of the vena terminalis which follows the curve of the caudate nucleus

The cerebrospinal fluid is secreted by the choroid plexus into the ventricles and is absorbed by the pacchionian granulations It circulates slowly through the lateral ventricles and the foramina of Monro into the third ventricle Thence it passes through the aqueduct of Sylvius to the fourth ventricle Through the lateral foramina of Luschka and the median foramen of Magendie it enters the subarachnoid spaces of the brain and spinal cord

Anatomical Basis of Memory

Memory is a function of all of the cerebral cortical neurons concerned with secondary and tertiary elaborations of sensory impressions and of all cortical areas concerned with association The primary cortical areas *of perception* do not seem to possess the function of memory because destruction of areas 17 and 42 (vision and hearing respectively) leaves the affected person blind and deaf but with intact memory for all visual and auditory impressions The prefrontal cortex may be destroyed without impairing memory it appears to lack the function of memory but able to utilize memories for the benefit of the organism

Memory usually is considered a psychological function but by a simple syllogism it can be made evident that psychology is merely a branch of cerebral

physiology Thus by definition all cerebral function is cerebral physiology Psychology is a cerebral function the brain is the organ of the mind as H Charleton Bastian elaborated Therefore psychology is a branch of cerebral physiology The only reason for any confusion has been that cerebral physiology has embraced all cerebral functions which were understood and the term psychology has been reserved for cerebral functions of so involved a character that man could not grasp them Memory is now within the realm of physiology even in the classical sense

Everyone will grant that when one perceives an object he ' makes a mental note ' of it When he sees it again he recognizes it Further when he performs an act or even a movement he recalls later how he did it That means that he has a memory of it Physiologically speaking when he sees an object the impulses set up by the seeing travel over certain neuronal pathways and when he sees the same object again and recognizes it impulses travel over the same pathways Those pathways are then called engrams traveled neuronal pathways and the engrams are the anatomical basis of memory of the seeing Similarly when he performs an act he utilizes certain engrams and those engrams are the anatomical basis of memory of the act

Now any act is performed more easily the second time than the first and still more easily in subsequent attempts A change must occur in the engram the first time it is used and also in subsequent functional activity That change is the record of the performance and the anatomical basis of memory It is probable that the changes are in the synapse to a greater degree than in the neuronal body or its projections and the change is probably at first chemical then physical and anatomical

If we apply this line of thought to Pavlov's[19] conditioned reflexes we can see an anatomical basis for the psychological behavior of the subject of his experiments Thus the ringing of a certain bell or an identical bell comes to signify food The dog will cock his head turn his eyes and watch then prepare to receive food all in response to a sound which he recognizes in his temporal lobe The desire for food is a state of unsatisfaction in the diencephalon When he feels that state hunger the sound is a signal that the hunger can be satisfied If he has just eaten he does not respond according to the same pattern But if he responds the pathways can be traced as follows Sound waves stimulate the tympanic membrane impulses travel via the cochlear nerve and a neuronal chain to the median geniculate bodies then to the gyri of the temporal lobes for perception of the vibration rate The adjacent cortical area where memories of identical sounds have been stored recognizes the sound as identical with others which preceded satisfaction of hunger Reflex impulses go over pathways to the quadrigeminal plate where appropriate movements of head and eyes take place By

cerebrals and a similar margin in the posterior and inferior portions, which is upplied by the po terior cerebral arteries The mesial surface of the hemispheres is supplied entirely by the anterior and posterior cerebral arteries The inferior surface of the temporal lobes and nearly all of the occipital lobes receive their blood supply from the posterior cerebral arteries The brain stem and cerebellum (surfaces and interior) receive their supply through branches of the basilar and posterior cerebral arteries

The anterior choroidal artery is a fairly large branch of the middle cerebral artery which turns backward to supply much of the choroid plexus of the lateral ventricle Its importance lies in the fact that it also supplies part of the thalamus nd the posterior portion of the internal capsule A lesion of it causes a focus of oftening illustrated at 5 in Fig 18

The general rule applies that the surface arteries unless they are the seat of aneurysms, or unless they are traumatized hardly ever rupture On the other hand they are subject to thrombosis The arteries, which receive part of their support from the brain substance are the ones which commonly rupture

The surface venous drainage of the cerebrum takes place in two directions, upward to the superior sagittal sinus and downward to the lateral and sigmoid inuses The deep drainage from the ventricles is through the deep cerebral veins, vein of Galen and straight sinus to the torcular The lateral ventricles are drained by means of the vena terminalis which follows the curve of the caudate nucleus

The cerebrospinal fluid is secreted by the choroid plexus into the ventricles and is absorbed by the pacchionian granulations It circulates slowly through the lateral ventricles and the foramina of Monro into the third ventricle Thence it passes through the aqueduct of Sylvius to the fourth ventricle Through the lateral foramina of Luschka and the median foramen of Magendie it enters the subarachnoid spaces of the brain and pinal cord

Anatomical Basis of Memory

Memory is a function of all of the cerebral cortical neurons concerned with econdary and tertiary elaborations of sensory impressions and of all cortical areas concerned with association The primary cortical areas *of perception* do not seem to possess the function of memory because destruction of areas 17 and 22 (vision and hearing respectively) leaves the affected person blind and deaf but with intact memory for all visual and auditory impressions The prefrontal cortex may be destroyed without impairing memory it appears to lack the function of memory but able to utilize memories for the benefit of the organism

Memory usually is considered a psychological function but by a simple syllogism it can be made evident that pyschology is merely a branch of cerebral

have a similar effect In other words visual hallucinations can result only from stimulation of the area for visual recall auditory hallucinations can result only from stimulation of the area for auditory recall From these facts as able a psychologist as McDougall and as able a neurologist as Henschen are agreed that all hallucinations result only from stimulation of the appropriate cortical area The timulus may result from a toxemia a neoplasm an abscess a circulatory dis *turbance or from an electrical stimulation It may be motivated from the* hypothalamus and hence result from an emotional disturbance

This is not the place to elaborate on this subject in detail but it is the firm conviction of the writer that eventually all psychiatric manifestations will be comprehensible on the basis of cerebral physiology

Spontaneous Electrical Activity of the Cortex

Over a period of many years Hans Berger of Jena studied by means of relatively crude apparatus certain electrical discharges from the cerebral cortex The enormous technical difficulties in the work may be judged by the fact that up to about 1935 a full time physicist specializing in electronics was required to maintain in good condition any such machine in daily active use

Berger discovered that a certain basal condition is essential to the recording of orderly waves whose interpretation i possible That state is one of es ential mental rest with eyes closed but without sleep Berger named the waves alpha beta gamma and delta waves At present the alpha rhythm still is called Berger rhythm but the other terms have largely fallen into disuse a terminology ba ed on frequency and amplitude having replaced the literal designation

Alpha waves are predominantly occipital waves of about 10 per second rate and 10 to 75 millivolt amplitude Beta waves are those about 25 per second frequency and 10 to 15 millivolt amplitude Gamma waves are rapid and small waves delta waves slow and large as well as irregular

Berger himself showed that the electrical waves at birth were irregular and slow and that only with development did the adult pattern appear (at an age between 9 and 15 years) (Fig 22) This harmonizes with the known facts of cerebral myelination Gibbs and Gibbs have issued a valuable atlas of electro encephalography to which the interested reader is referred for details

As stated previously Abrador and Kennard independently have shown that all brain waves are extinguished upon complete destruction of the hypothalamus The function of attention has an enormous influence on the waves the mere opening of the eyes (visual attention) obliterates the occipital alpha rhythm Demonstrators have shown upon themselves that enormous variability in waves at the moment being recorded can be produced by voluntary thinking of various

way of the tect rinal pathways impulses go to the spinal cord to give the dog his appropriate reflex support as he shifts the weight of his body and as he turns his head and prepares to walk toward or to the food Simultaneously im pul es go to the occipital lobe to awaken memory of the appearance of the food All of the cortical areas stimulated send impulses to and receive impulses from the diencephalon The hypothalamic centers for salivary and gastric secretion are stimulated and impulses travel over the vegetative nervous system to the glands in question Ordinarily this train of events is described as ' sound of the bell start glandular secretion and the phenomenon is called psychic con ditioning

Neurological Basis of Psychiatry

In harmony with the ancients in 1890 H Charleton Bastian the English neu rologist as mentioned, assembled enough material to conclude that " the brain is the organ of the mind With the advent of the sciences of vegetative neurology and of endocrinology a tendency to doubt Bastian s thesis developed It was clearly shown that pituitary and thyroid disturbances could easily upset the function of ' the mind ' to the extent of cau ing mental derangement However, with more extensive knowledge and more intensive study it has become increas ingly evident that the brain *actually is the organ of the mind* Pituitary dis turbances which cause mental derangement can result also from hypothalamic neuronal disease affecting the pituitary gland and thyroid disturbances, when they cause mental symptoms act by causing a toxemia which in turn affects the brain

As already indicated disturbances of certain regions of the hypothalamus may cause stupor of others hypomanic excitement Foerster has shown that mere gentle mechanical stimulation of the *floor of the* third ventricle may cau e hypo manic activity with disturbance of judgment lasting as long as the duration of the mechanical stimulation

It is well established experimentally as well as clinico pathologically that cer tain well delineated areas of the cerebral *cortex* are concerned with perception with recognition and with recall of visual auditory and tactile impulses The areas for taste and smell are not so definitely *known* For the zones which are well known it is fully established that the areas for perception if stimulated will cause the patient to perceive the stimulus as specific for that modality of sensa tion The areas for recognition will when stimulated give rise to recognition of specific stimuli and those for recall will arouse *recall* Thus if the visual area of recall is stimulated the patient will see an object which he has seen formerly, even though the stimulus is electrical That is another way of saying that he will have a visual hallucination Stimulation of any other area of the brain will not

have a similar effect In other words visual hallucinations can result only from stimulation of the area for visual recall auditory hallucinations can result only from stimulation of the area for auditory recall From these facts as able a psychologist as McDougall and as able a neurologist as Henschen are agreed that all hallucinations result only from stimulation of the appropriate cortical area The stimulus may result from a toxemia a neoplasm an abscess a circulatory disturbance or from an electrical stimulation It may be motivated from the hypothalamus and hence result from an emotional disturbance

This is not the place to elaborate on this subject in detail but it is the firm conviction of the writer that eventually all psychiatric manifestations will be comprehensible on the basis of cerebral physiology

Spontaneous Electrical Activity of the Cortex

Over a period of many years Hans Berger of Jena studied by means of relatively crude apparatus certain electrical discharges from the cerebral cortex The enormous technical difficulties in the work may be judged by the fact that *up to about 1935 a full time physicist specializing in electronics was required to* maintain in good condition any such machine in daily active use

Berger discovered that a certain basal condition is essential to the recording of orderly waves whose interpretation is possible That state is one of essential mental rest with eyes closed but without sleep Berger named the waves alpha beta gamma and delta waves At present the alpha rhythm still is called Berger rhythm but the other terms have largely fallen into disuse a terminology based on frequency and amplitude having replaced the literal designation

Alpha waves are predominantly occipital waves of about 10 per second rate and 10 to 75 millivolt amplitude Beta waves are those about 25 per second *frequency and 10 to 15* millivolt amplitude Gamma waves are rapid and small waves delta waves slow and large as well as irregular

Berger himself showed that the electrical waves at birth were irregular and slow and that only with development did the adult pattern appear (at an age between 9 and 15 years) (Fig 22) This harmonizes with the known facts of cerebral myelination Gibbs and Gibbs have issued a valuable atlas of electro encephalography to which the interested reader is referred for detail

As stated previously Abrador and Kennard independently have shown that all brain waves are extinguished upon complete destruction of the hypothalamus The function of attention has an enormous influence on the waves the mere opening of the eyes (visual attention) obliterates the occipital alpha rhythm Demonstrators have shown upon themselves that enormous variability in waves at the moment being recorded can be produced by voluntary thinking of various

situations Gibbs and Gibbs[14] state (page 50) that "The most extreme ab normalities in the electroencephalogram may be unassociated with any clinical disorder, and on the other hand a patient may have a clinical history of frequent seizures and yet show little in the way of interseizure disorder He may even

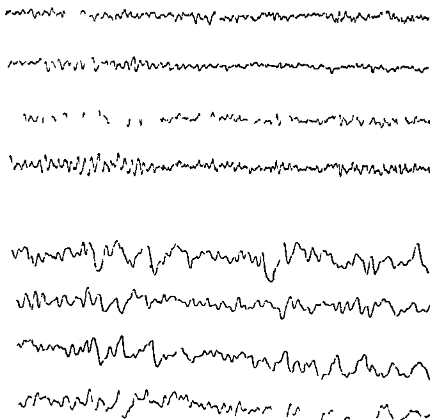


FIG 2 Normal electroencephalogram above Disturbances below after electroshock Four simultaneous tracings were taken

have focal seizures involving one side of the face without loss of consciousness and show no change in the electroencephalogram Nevertheless properly interpreted, electroencephalograms are of great clinical value in neurology

The writer would like to comment on the expression unassociated with any clinical disorder' Many conditions of the brain obviously due to disease upon microscopic examination can be present without clinical evidence of disease Thus the residuals of partial asphyxia at birth tiny lesions due to rheumatic disease those due to pertussis and other cellular abnormalities of vague etiology

may ea ily be present without definable clinical manifestations Thus when one speaks of variability in normal electroencephalograms one may be in con siderable error in defining the normal Electroencephalography still is too young a science to justify dogmatic statements concerning interpretations

BIBLIOGRAPHY

1 RAMON Y CAJAL S Histology Wm Wood and Co Baltimore 1933
2 ADRIAN E C Conduction in peripheral nerves and in the central nervous sys tem Brain 1918 XLI 23
3 SHERRINGTON C S The Integrative Action of the Nervous System C Scrib ner s Sons New York 1906
4 FULTON J F Physiology of the Nervous System nd ed Oxford Univ Pre s New York 1943
5 TOWER S S Pyramidal and extrapyramidal me hani ms in the cortical control of movement Meeting of Phila Neurol Soc Oct 23 194 Arch Neurol and Psychiat 1943 XLIX ,82 also in BUCY P C The Precentral Motor Cortex Univ Ill Press Urbana 1944
6 HINES M in BUCY P C The Precentral Motor Cortex Univ Ill Press Urbana 1944
, LARSELL O The cerebellum a review and interpretation Arch Neurol and Psychiat 193 XXXVIII 580
8 BAILEY P and DAVIS E W Effects of lesions of periaqueductal gray matter in cat Proceed Soc Exper Biol and Med 1942 LI 51
9 RADEMAKER G G J Die Bedeutung der roten Kerne und des ubrigen Mittel hirns fur Muskeltonus Korperstellung und Labyrinthreflexe Monographie au dem Gesamtgebiete der Neurologie und Psychiatrie D Foerster und K Wilmanns Heft 44 Berlin 1926
10 SPATZ H Handbuch der Neurologie Bumke Foerster Sprin er I 4,4 Berlin 1935
11 OBRADOR S Effect of hypothalamic lesions on electrical activity of cerebral cortex Jour Neurophysiol 1943 VI 81
12 KENNARD M A Effects on EEG of chronic lesions of ba al ganglia thalamus and hypothalamus of monkeys Jour Neurophy iol 1941 VI 40
13 MASSERMAN J H Behavior and Neuro is Univ of Chicago Press Chicago 1943
14 GIBBS F A and GIBBS E L Atlas of Electroencephalography Publi hed by the Authors Cambridge Mass 1941
15 ALPERS B J Personality and emotional disorders associated with hypothalami lesions Assoc Research Nerv and Ment Dis Chap XXVIII p 5 William and Wilkins Co Baltimore 1940
16 FOERSTER O Handbuch der Neurologie Bumke Foerster Vol VI Springer Berlin 1936

1, BUCY P C The Pericentral Motor Cortex U I I Pr Urbana 1944
18 STERN K Severe dementia associated with r l symmetrical degeneration of the thalamus Brain 1939 LXII 15
19 CLARK W E L BEATTIE J RIDDOCH G I I I N M The Hypothalamus Morphological Functional Clin l and Surg l Aspects Oliver and Boyd London 1938
o PAPEZ J W Summary of finer connection h each other and with other portions of the brain Assoc Re rch N r a Ment Dis 194 XXI 1
1 WALKER A E The Primate Thalamus Chicago U n Pre ago 1938
JACOB A Die extrapyramidalen Erkrankungen Springer Be 19 3
3 WILSON S A K An experimental research into the anat and physiology of the corpus striatum Brain 1913-1914 XXXVI 4
4 VON ECONOMO C and KOSKINAS G N Die Cytoarkitektonik der Hirnrinde der erwachsenen Menschen Springer Berlin 19 5
5 BAILEY P VON BONIN G and ASSOCIATES Functional organization of medial aspect of primate cortex Jour Neurophysiol 1944 VII 1
6 JACKSON J H Selected Writings of ed by J Taylor Hodder and Stoughton London 1931
7 GAROL H W and BUCY P C Suppression of motor response in man Arch Neurol and Psychiat 1944 LI 5 8
8 NIELSEN J M Aphasia Chap X Vol VI Oxford Med Oxford Univ Press New York 1944
9 NIELSEN J M Agnosia Apraxia Aphasia Los Angeles Neurological Society Los Angeles 1936 also in Textbook of Clinical Neurology Hoeber New York 1941
30 DUSSER DE BARENNE J G and McCULLOCH W S Suppression of motor respon e upon stimulation of areas 4-s of the cerebral cortex Proceed Am Phy iol Soc Apr 6-29 1939 Am Jour Physiol 1939 CXXVI 48
31 BAILEY P Unpublished work personal communication
3 HENSCHEN S W Klinische und anatomische Beitrage zur Pathologie des Gehirns Almquist and Wikoell Stockholm 19 0-19 2
33 NIELSEN J M Agnosia Apraxia Aphasia Hoeber New York 1945
34 KLEIST K Gehirnpathologie vornehmlich auf Grund der Kriegserfahrungen Johann Ambrosius Barth Leipzig 1934
35 BRICKNER R M The Intellectual Function of the Frontal Lobes a Study Ba ed upon Observation of a Man after Partial Bilateral Frontal Lobectomy Macmillan New York 19,6
36 FREEMAN W and WATTS J W Behavior and the frontal lobes Trans New York Acad Sci 1944 VI 84
3, MILL J S Harvard Cla sics Vol 6 Collier New York
38 BASTIAN H C The Brain as an Organ of Mind D Appleton and Co New York, 1880

39 PAVLOV I P Lectures on Conditioned Reflexes Translated by W Horsley Gantt International Publishers New York 19 8

40 BERGER H Über das Elektrenkephalogram des Menschen Arch f Psychiat XCIV 16 1931 a whole series of articles followed in various journals

December 1 1945

CHAPTER I-A

ELECTROENCEPHALOGRAPHY

By WILLIAM G. LENNOX

TABLE OF CONTENTS

NORMAL ELECTROENCEPHALOGRAMS

That the brain possesses electrical activity has been known since 1874. To Hans Berger of Jena and the year 1929 belongs the credit of demonstrating that these potentials could be led off through the intact human skull and recorded. Amplifying devices developed in radio research permit the building up of minute voltages which can then be made to trace a curve on film or on paper, either photographic or plain. Ink records on paper are used for clinical work for reasons of economy. For the patient the examination is simplicity itself. Electrodes are pasted to the scalp and the patient sits or lies quietly with eyes closed for fifteen minutes while his brain busily scribbles an account of its activity. The potentialities of this technique for a better understanding of the activity of the brain in man and animals are great. Its value to the clinician is limited by various factors: the initial cost of the apparatus and the unsatisfactory performance of certain types, the need for expert care in maintenance and for competent interpretation of records after they are made. The technique of electroencephalography, reproductions of a great

variety of records and a bibliography of references are given in the Atlas of Electroencephalography by Dr and Mrs F A Gibbs Jasper has written an excellent review from a neurosurgical laboratory

In normal persons who are awake the brain waves as they are popularly called form a wavy line with fluctuations which recur from eight and one half to twelve times per second and have a voltage from peak to trough of from ten to fifty millionths of a volt microvolts These waves represent the discharge of nuclei of neurons The configuration of the waves differs for different areas of the cortex and varies with the varying activity of the brain The most easily identified and constant of the rhythms is obtained from over the occipital area when the subject s eyes are closed This is called the alpha or Berger rhythm Waves with a frequency of from one to sixty cycles per second may be encountered in the record Very fast rhythms have been called beta and very slow ones delta but statement of the actual observed frequencies per second is more accurate and therefore preferable Both the frequency and the voltage of waves are important

Modifying Factors of Brain Waves

In the human subject the brain waves may be modified by a number of conditions An understanding of these is essential for the interpretation of records

Constitutional Factors — Study of the records of twins indicates that the pattern traced by the electrical waves of the cortex is an hereditary trait In the examination of 65 twins Lennox Gibbs and Gibbs found that identical twins without history of brain injury have brain waves which are indistinguishable whereas the brain waves of non identical twins differ This fact is of importance in the study of the genetics of brain waves particularly in conditions associated with unusual rhythms such as epilepsy In a group of 3?0 near relatives of epileptic patients 52 per cent had brain waves with some degree of abnormality and in 95 families in which both parents were tested the records of both parents were abnormal in 27 per cent one was abnormal in 54 per cent and neither was definitely abnormal in 19 per cent

Environmental Factors — Decision as to whether a person s cortical dysrhythmia was transmitted or acquired may be difficult unless brain wave records can be made of both parents and a clearcut history regarding brain injury, either positive or negative can be obtained The etiology of dysrhythmia is indicated most clearly in the case of identical twins If the records of these twins are unlike the conclusion seems

justified that the difference is due to some environmental influence Environmental conditions which alter brain waves may be physiological or pathological

Physiological Alterations — Acute changes of brain waves attend alterations in the activity of the brain The standard or basal conditions for making a record require the person to be awake his eyes closed and his mind and body relaxed Opening the eyes or visualizing with the eyes closed immediately causes increased frequency and decreased voltage of waves from the occipital areas so that the wave frequency is counted with more difficulty Apparently the increased activity of the optical tract imposes a faster frequency and interferes with the normal resting synchrony of the occipital area To a lesser degree voluntary attention or sensory stimuli which engage the attention increase frequency and lower voltage The onset of sleep is marked by faster lower waves and deep sleep by large three or four per second waves which if they occurred with the subject awake would be pronounced grossly abnormal Brain waves during involuntary sleep as from drugs or narcolepsy are similar to those of voluntary sleep Hypnosis resembles the waking rather than the sleeping state Attempts to correlate wave changes with thought or mood changes have not been rewarding Loss of consciousness from any cause is accompanied by brain rhythm which would be abnormal were the person conscious Maximum fatigue may be accompanied by abnormally slow waves

Chemical Changes — Alterations of brain waves which attend acute changes in the brain activity such as attention may be induced chemically a result of increased metabolic activity of the discharging cells In animals a correlation between the oxygen tension of the brain and the frequency of its electrical pulsations has been demonstrated In human subjects the relationship between the metabolism of the brain and brain waves has been studied by F L Gibbs and associates by means of the analysis of blood drawn simultaneously from an artery and an internal jugular vein while the subject s brain waves were being recorded Of the substances which have been measured the electrical activity of the brain is most readily influenced by changes in the carbon dioxide tension and the pH Decreased concentration of carbon dioxide of oxygen of glucose and an increased alkalinity of the blood passing through the brain causes a slowing of the brain waves and an increase of certain types of abnormal waves The opposite conditions cause a quickening of waves and an improvement of certain wave disorders Drugs which are convulsive or cause sleep have a profound effect on the brain waves smaller changes have been noted for various other types of drugs

Chronic or Long Range Alterations — Chronic or long range alterations of wave frequencies accompany growth and physiological cycles In the newborn child waves are but one half to two per second with voltages of from 20 to 50 microvolts with superimposed very fast low voltage waves The underlying rhythm gradually increases in frequency until by about the ninth year the record from the occipital area approximates that of the adult although other areas remain relatively slow The low voltage fast record encountered in 12 per cent of normal adults is seldom seen before the fourteenth year By the nineteenth year records are fully adult The aged tend to have either abnormally fast or slow waves Paradoxically dysrhythmia occurs less frequently in elderly than in youthful epileptics although this may represent the survival of the rhythmic Probably slight differences mark the sexes and slight changes accompany the menstrual cycle Waves become faster or slower with respectively increased or decreased basal metabolic rates and with increased or decreased body temperature

Abnormal Electroencephalograms

The physician is most interested in the concurrence of abnormal waves and abnormal physical or mental behavior These two groups do not exactly coincide for a few normal persons have abnormal brain waves and many abnormally behaving persons have normal waves The degree of coincidence and the significance of various kinds of wave patterns can be judged by comparing the records of a sample of the population with the records of large groups of persons suffering from certain disorders of the central nervous system

The Gibbs have classified the records of 1 260 epileptics and of 1 000 adult controls placing each record in one of eighteen groups Samples of these eighteen tracings are shown in Fig 1 together with their percentage distribution in the control group Of the 1 000 records 84 4 per cent have waves which are fast but of such low voltage that they cannot be counted or else have a dominant frequency between 8 5 and 12 per second These are classed as normal The waves of 13 8 per cent are somewhat faster or slower and of 1 1 per cent are much faster or slower than the limits specified In 0 9 per cent the records contain occasional paroxysmal discharges of high voltage waves (marked petit mal and psychomotor in Fig 1) These are called seizure discharges because they resemble the tracings recorded during the various kinds of epileptic seizures The types of abnormal records do not have equal pathological significance In a group of 730 adult epileptics records

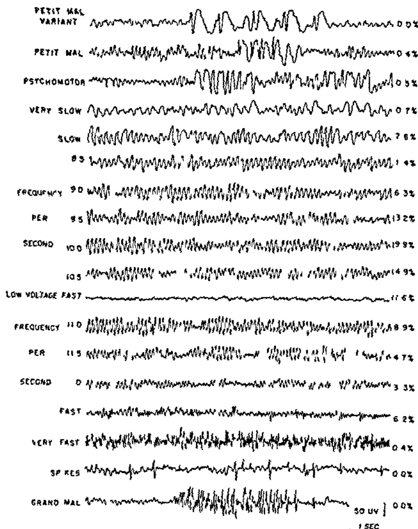


Fig 1 Clas ificati n of electroencephal grams use l by the Gibbs Electroencephalograms are placed by them in 18 cla se 15 of these were encountered in 1 000 contr l adult th percent occurrence being ind cated by the figures at the right of the tracings thr e the first and la t two marked at right 0 0 are abnormal tracing n t encountered *in the 1 000 contr l adult* The e with 6 ther *tracing making up 15 per cent* of the total encountered in the 1 000 contr l a lults are considered abn rmal In Fig 1 then the five upper and the four lower trac ng are consi l red as bn rmal th other nine as normal At the b tt m of the r ght hand corner i th signal ma ke l b made by 50 micro volts an l the t me interval of one second Fig 1 i from Gibbs F A Gibbs E L and Lennox W G Arch Neurol and Psychiat arti le now in pres

with paroxysmal discharges of high voltage waves occurred 34 times more frequently very slow or very fast waves 17 times more frequently and slightly slow or fast waves only 2 times more frequently than in the control group Further description of the electroencephalographic findings in epilepsy appear under that heading (see Oxford Medicine Vol VI Chapt XXX)

Patho physiology

Disorders of the electrical pulsation of the brain may occur with or without demonstrable pathology or structural alterations of the brain Abnormal pulsations probably represent some abnormality in the chemical makeup or reactions of the neurones of the brain or else some disturbance in the integration of nerve cell activity The fact that brain waves are altered so easily by changes in the chemistry of the blood flowing through the brain speaks for a direct chemical action As has been intimated this abnormal state or reaction may be an inborn characteristic the product of a certain gene molecule or it may be an acquired characteristic the result of environmental chemical or structural changes Genetic (essential) epilepsy is the clearest example of an hereditary cerebral dysrhythmia Distinction between dysrhythmia which is based on metabolic or on organic disorders of the brain is not always possible

In the metabolic group probably belong the bradyrhythmia of myxedema and the dysrhythmia of diabetes of thiamine deficiency and of Addison s disease These and other acute medical conditions have been studied insufficiently Of especial interest are those in which loss of consciousness or convulsions may be a symptom Psychoneurosis and hysterical seizures are not associated with disturbances of brain waves although an hysterical person like a normal person may have dysrhythmia Loss of consciousness from cerebral anemia as in syncope and in the non cerebral type of the carotid sinus reaction are accompanied by slow high voltage waves The eclampsia which occurs in certain cases of toxemia of pregnancy may be due to a pre existing dysrhythmia Fever causes an increased speed of brain waves In spite of its genetic linkage with epilepsy the seizures of migraine are not accompanied by electrical brain storms perhaps because the commotion is in the sympathetic nervous system However some degree of abnormality is at least twice as frequent in migraine patients as in the control group The same statement can be made of persons with some aberration of behavior inmates of prisons or behavior problem children The distribution of wave patterns among persons of genius or of distinction needs to be ascertained

Besides the acute changes in body physiology which have been mentioned the brain may suffer direct injury with an accompanying disturbance of brain waves which may be reversible or irreversible In the treatment of schizophrenia the administration of a convulsant drug or electric shock produces abnormal wave patterns which tend to subside in the course of weeks or months The same may be said of infections which involve the cerebrum brain abscess or edema encephalitis Sydenham s chorea and meningitis Trauma of the brain tumors foreign bodies and subdural hematomas produce localized disturbances which tend to persist as long as the pathology remains or perhaps even spread and become generalized in persons who later will develop convulsions It must be remembered that subcortical lesions as in Parkinson s disease mid brain hemorrhages or lesions involving the cerebellum may not be accompanied by demonstrable disorder of the electroencephalogram as ordinarily taken Electroencephalography is intriguing because of its negative as well as its positive testimony Sections of the brain may be amputated or extensive subcortical injuries may take place and the electroencephalographer be none the wiser

Cortical Localizations

For ordinary diagnostic purposes a monopolar arrangement is used one electrode on the head the other on the lobe of the ear The curve obtained represents the fluctuating electrical activity of the cortex in the region of the head electrode With an apparatus which writes six simultaneous curves an experienced person may detect a focus of abnormal discharge by noting the appearance of high voltage waves consistently in one or more of the curves

A technique of localizing cortical lesions was used first by Walter In this method both electrodes bipolar leads are placed on the head If the waves between these electrodes are the reverse of the waves between two adjacent electrodes an out of phase relationship the lesion or its periphery lies between the two pairs In practice sixteen placements of electrodes are used and various adjacent regions are compared In order to gain information about abnormal discharges in regions other than the cortex electrodes have been placed in the nasopharynx in the cisterna magnum and in the brain itself Used in conjunction with neurological examinations and pneumoencephalograms electroencephalography is a great aid to the neurosurgeon Of further aid to him is the classification of records used by Jasper This author also pointed out the significance of diphasic spikes in areas of organic lesions

with paroxysmal discharges of high voltage waves occurred 34 times more frequently very slow or very fast waves 17 times more frequently and slightly slow or fast waves only 2 times more frequently than in the control group Further description of the electroencephalographic findings in epilepsy appear under that heading (see Oxford Medicine Vol VI Chapt XXX)

Patho physiology

Disorders of the electrical pulsation of the brain may occur with or without demonstrable pathology or structural alterations of the brain Abnormal pulsations probably represent some abnormality in the chemical makeup or reactions of the neurones of the brain or else some disturbance in the integration of nerve cell activity The fact that brain waves are altered so easily by changes in the chemistry of the blood flowing through the brain speaks for a direct chemical action As has been intimated this abnormal state or reaction may be an inborn characteristic the product of a certain gene molecule or it may be an acquired characteristic the result of environmental chemical or structural changes Genetic (essential) epilepsy is the clearest example of an hereditary cerebral dysrhythmia Distinction between dysrhythmia which is based on metabolic or on organic disorders of the brain is not always possible

In the metabolic group probably belong the bradyrhythmia of myxedema and the dysrhythmia of diabetes of thiamine deficiency and of Addison s disease These and other acute medical conditions have been studied insufficiently Of especial interest are those in which loss of consciousness or convulsions may be a symptom Psychoneurosis and hysterical seizures are not associated with disturbances of brain waves although an hysterical person like a normal person may have dysrhythmia Loss of consciousness from cerebral anemia as in syncope and in the non cerebral type of the carotid sinus reaction are accompanied by slow high voltage waves The eclampsia which occurs in certain cases of toxemia of pregnancy may be due to a pre existing dysrhythmia Fever causes an increased speed of brain waves In spite of its genetic linkage with epilepsy the seizures of migraine are not accompanied by electrical brain storms perhaps because the commotion is in the sympathetic nervous system However some degree of abnormality is at least twice as frequent in migraine patients as in the control group The same statement can be made of persons with some aberration of behavior inmates of prisons or behavior problem children The distribution of wave patterns among persons of genius or of distinction needs to be ascertained

Besides the acute changes in body physiology which have been mentioned the brain may suffer direct injury with an accompanying disturbance of brain waves which may be reversible or irreversible In the treatment of schizophrenia the administration of a convulsant drug or electric shock produces abnormal wave patterns which tend to subside in the course of weeks or months The same may be said of infections which involve the cerebrum brain abscess or edema encephalitis Sydenham s chorea and meningitis Trauma of the brain tumors foreign bodies and subdural hematomas produce localized disturbances which tend to persist as long as the pathology remains or perhaps even spread and become generalized in persons who later will develop convulsions It must be remembered that subcortical lesions as in Parkinson s disease and brain hemorrhages or lesions involving the cerebellum may not be accompanied by demonstrable disorder of the electroencephalogram as ordinarily taken Electroencephalography is intriguing because of its negative as well as its positive testimony Sections of the brain may be amputated or extensive subcortical injuries may take place and the electroencephalographer be none the wiser

Cortical Localizations

For ordinary diagnostic purposes a monopolar arrangement is used one electrode on the head the other on the lobe of the ear The curve obtained represents the fluctuating electrical activity of the cortex in the region of the head electrode With an apparatus which writes six simultaneous curves an experienced person may detect a focus of abnormal discharge by noting the appearance of high voltage waves consistently in one or more of the curves

A technique of localizing cortical lesions was used first by Walter In this method both electrodes bipolar leads are placed on the head If the waves between these electrodes are the reverse of the waves between two adjacent electrodes in out of phase relationship the lesion or its periphery lies between the two pairs In practice sixteen placements of electrodes are used and various adjacent regions are compared In order to gain information about abnormal discharges in regions other than the cortex electrodes have been placed in the nasopharynx in the cisterna magnum and in the brain itself Used in conjunction with neurological examinations and pneumoencephalograms electroencephalography is a great aid to the neurosurgeon Of further aid to him is the classification of records used by Jasper This author also pointed out the significance of diphasic spikes in areas of organic lesions

Mental States

Because of the importance of the mind in relation to brain activity the lack of dramatic correlations between mentality and brain waves is nonplusing Encephalograms of the higher animals are as good as those of humans There seems to be no correlation between intelligence quotients and the electroencephalogram The feebleminded usually have normal records on the other hand those of deteriorated epileptics are grossly slow The majority of patients with general paresis have abnormal records the proportion being higher in those with seizures The mental decay which attends Schilder's disease and chronic encephalopathies of the aged is associated with much dysrhythmia

In the case of the major psychoses the testimony is mixed In manic depressive psychosis the evidence is indecisive In schizophrenia abnormalities occur several times more frequently than in control groups but they are not concentrated in one type of pattern

THE FUTURE OF ELECTROENCEPHALOGRAPHY

Fundamental experimental work on the pathway of nervous discharges and on the relationship between the metabolic and the electrical activity of the brain is now possible A wide survey must be undertaken of the brain wave patterns in many samples of the population both normal and abnormal but especially in persons with a disturbance of nerve function of mentality or of behavior Most intriguing is the possibility of prevention by means of eugenics of those mental and neurological diseases which are associated with an hereditary cerebral dysrhythmia

BIBLIOGRAPHY

BERGER H Ueber das Elektrenkephalogramm des Menschen Arch Psychiat 1929 LXXXVII 5[illegible]9

GIBBS F A and GIBBS E L Atlas of Electroencephalography A Cummings Cambridge Mass 1941

GIBBS F A GIBBS E L and LENNOX W G Electroencephalographic classification of epileptics and controls Arch Neurol and Psychiat, in press

JASPER H A Electroencephalography Chapter XIV in Epilepsy and Cerebral Localization by Penfield W and Erickson T C Charles C Thomas Springfield Ill 1941

March 1 1943

CHAPTER II

VASCULAR DISTURBANCES

By L. FARQUHAR BUZZARD

Table of Contents

General Considerations

Anatomical.—Arterial blood is supplied to the contents of the skull mainly by the two vertebral and the two internal carotid arteries. These four vessels combine to form a large arterial plexus at the base of the brain generally known as the circle of Willis, from which branches are distributed to the whole of both hemispheres. The vertebral arteries and the basilar artery, formed by their union, are mainly responsible for the blood supply

of the pons medulla and cerebellum They take a part in the distribution of blood to the hemispheres through the posterior cerebral arteries which also receive a contribution from the carotid system through the posterior communicating arteries From the circle of Willis arise two groups of vessels (a) a number of branches leaving the main trunks at a right angle and penetrating the substance of the brain to reach important central structures such as the basal ganglia and the internal capsules and (b) a number of vessels which spread themselves over the surface of the hemispheres breaking up into smaller and smaller branches in the meshes of the pia and sending countless offshoots into the cortex Some of the latter terminate in the gray matter others are of greater length and penetrate the white matter of the centrum ovale to reach the basal ganglia In this way the territories supplied by each group incline to overlap but there seems to be no real anastomosis between the two sets of vessels

The anterior middle and posterior cerebral arteries the three important arterial trees springing from the circle of Willis are responsible for the blood supply of the cortex Although their areas of distribution are more or less defined there is some overlapping and some anastomosis between small twigs belonging to adjacent branches of different parentage

From deep seated capillaries the blood is returned by small veins to a venous plexus on the surface of the brain This plexus empties itself through the agency of larger vessels into the venous sinuses which lie in folds of the dura mater and which have intimate connections with each other The large venous lake formed by the sinuses is drained almost entirely by the two internal jugular veins but there exist numerous though small channels of communication with the veins on the outer side of the skull Of these channels the veins of the orbit and those of the diploe are the most important In this way does intracranial venous congestion become portrayed in the face

Physiological—The physiological principles which govern the cerebral circulation are still so imperfectly determined that the interpretation of pathological disturbances can only be a matter of surmise According to modern teaching the cerebral circulation is controlled by the same influences as the circulation in other parts of the body Thus the brain dilates with each cardiac beat and its blood content varies slightly with respiration During inspiration blood is sucked into the thoracic cavity and during expiration the venous outflow from the skull is impeded But the total amount of blood within the skull can vary but little inasmuch as the only other variable intracranial content the cerebrospinal fluid has but a small volume The variations which take place are in the relative amounts of arterial and venous blood an increase in one being associated with a corresponding decrease in the other The venous sinuses share in a general

venous congestion which affects the whole body such as that which follows prolonged expiratory efforts On the other hand the brain shares in the general arterial hyperemia associated with a rise in the blood pressure

The existence of a vasomotor mechanism controlling the cerebral circulation independent of the general circulation has long been a matter of dispute and the justification for regarding certain clinical phenomena as the result of a local vasomotor constriction or dilatation must depend on the final answer to this question The facts that the cerebral arteries have muscular coats supplied by nerve fibers that stimulation of the cervical sympathetic produces vascular changes in the brain and that certain drugs such as adrenalin can produce local results support the view that the cerebral circulation may be regulated to some extent by a vasomotor mechanism of its own

Cerebral Hyperemia

Although a large increase in the volume of blood in the cerebral vessel is not possible an arterial hyperemia is recognized as a natural sequel to an increase of the general blood pressure More arterial blood than usual passes through the brain in a given time and unless this is associated with some morbid process such as the presence of a tumor or grave arterial disease the results are physiological rather than pathological Mental activity is increased and a sense of well being may be experienced On the other hand a rise in blood pressure in the presence of increased intracranial pressure resulting from cerebral tumor hydrocephalus uremia or cerebral hemorrhage may bring about distressing and even dangerous symptoms in the form of headache slowing of respiration and disturbances of consciousness

A venous hyperemia is the result of impeded outflow from the venous sinuses and in mild degrees may not give rise to symptoms If continued for any length of time the brain must suffer from the corresponding decrease of arterial blood and the picture presented is that of cerebral anemia with giddiness faintness clouding of consciousness and possibly convulsions

Cerebral Anemia

This may be general or local The results of general anemia are very similar whether they are produced by a diminution of the arterial supply or by venous congestion as described above A diminished supply of arterial blood may be brought about by cardiac failure by bleeding or by determination of the blood to the abdomen such as follows the rapid removal

of a large quantity of ascitic fluid When cerebral anemia is rapidly or suddenly produced loss of consciousness is the primary consequence and this may be followed by convulsions slowing of pulse and respiration dilatation of the pupils and rise of blood pressure A continued state of anemia leads to an increase in the pulse rate associated with a fall of pressure and failure of respiration

The pathological changes associated with anemia have been studied in animals A dog may survive the simultaneous ligation of both carotid and both vertebral arteries but it presents a condition of idiocy and examination of the cortex reveals definite changes in the nerve cells They become swollen stain diffusely with methylene blue and lose their Nissl granules A monkey does not survive a similar operation and in man the ligation of one carotid artery is not always a safe operation Cerebral anemia brought about gradually, also leads to definite changes in the nervous elements of the brain as is seen in cases of progressive double hemiplegia, the result of widespread cerebral arteriosclerosis In such cases the cortical cells become atrophied and the nerve tracts degenerate

Local anemia of the brain frequently occurs as a sequel to arterial thrombosis or embolism and the consequences will be described later In order to explain certain clinical phenomena in the form of transient hemiplegias monoplegias or hemianopias the possibility of a local anemia following local vasoconstriction has been entertained but no confirmation of this hypothesis is yet available

Lesions of Cerebral Vessels

Etiology

Thrombosis —The formation of a thrombus within the lumen of a cerebral artery probably never occurs except as the result of embolus or of disease of the vessel wall The etiology of embolism will be considered later

The arterial disease may be acute subacute or chronic Acute arteritis is the result of some infective process which may be limited to the vessel or which may involve the surrounding tissues as well Thus arteritis with thrombosis is a rare complication of some of the acute specific fevers such as enteric fever scarlet fever diphtheria and possibly pneumonia On the other hand encephalitis of whatever origin is a potent source of arteritis especially in connection with the smaller arteries and secondary thrombosis is a common result This has been well demonstrated in fatal cases of lethargic encephalitis and it is probable that similar effects are produced by the encephalitis of infancy due to the virus of poliomyelitis It is not unreasonable to suppose that an inflammatory thrombosis of this nature is partly responsible at any rate for many cases of infantile hemiplegia

Subacute arteritis is most frequently the result of syphilis and the gummatous changes in the arterial walls generally lead to thrombosis (Fig 1) The middle cerebral artery and its branches appear to be peculiarly liable to this process but the branches of the basilar artery and of the other cerebral arteries are by no means immune A tuberculous meningo arteritis is sometimes responsible for thrombosis of one of the cerebral arteries

Chronic arteritis or atheroma is the most common etiological factor in the production of thrombosis especially when it is accompanied by an increase in the coagulability of the blood or by a fall of the blood pressure The middle cerebral artery is again more prone to be involved in lesions of this kind

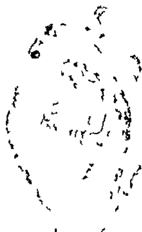


Fig 1 —Section of middle cerebral artery showing arteritis thrombosis and organization of the thrombus from a case of gummatous arteritis of both middle cerebral arteries

The acute infective forms of arteritis are more frequent in young persons while atheroma is rare before fifty years of age Between twenty and forty years of age cerebral thrombosis is nearly always the result of gummatous arteritis

Venous thrombosis is a comparatively rare occurrence and is usually a part of an acute infective process or more rarely associated with abnormal blood states such as chlorosis

Embolism — An embolus in the cerebral circulation may be a mass of fibrin a piece of diseased cardiac valve or possibly a detached portion of the intima of the aorta or of its main branches It brings about an arrest of circulation and thrombosis by becoming lodged at an arterial bifurcation most frequently in the branches of the middle cerebral artery on the left side of the brain

Cerebral embolism is a circulatory accident which commonly occurs in young adults who are suffering from mitral stenosis In cases of infective endocarditis the embolus may be the carrier of organisms to the brain and the infarcted area may become infected with the result that an abscess is formed

Hemorrhage —The rupture of an artery is a much more frequent source of intracranial hemorrhage than the rupture of a vein an extravasation of venous blood being almost always the result of some kind of injury The essential condition of arterial hemorrhage is disease or trauma of the vessel

wall and it is a matter of some dispute as to whether a healthy artery ever ruptures except as the result of violence The chief exciting cause of hemorrhage is a rise in the arterial blood pressure with or without a coincident venous congestion Cerebral hemorrhage is rare under forty years of age and becomes increasingly common after the prime of life is past It is more frequent in men than in women

Arterial or venous extravasation may be the result of birth injuries and so play an important part in the production of congenital hemiplegias or of diplegias In childhood hemorrhage is probably an accident occurring in the course of an encephalitis except when it follows an injury to the head Possibly a few cases result from the excessive strain put upon the cerebral vessels in the course of whooping cough During a paroxysm of coughing venous pressure is raised by expiratory efforts and arterial pressure is increased by muscular exertion

Between thirty and forty years of age syphilitic arteritis may occasionally be responsible for cerebral hemorrhage but the large majority of cases are due to trauma Atheroma and arteriosclerosis associated with granular kidney and hypertrophy of the left ventricle of the heart are the conditions which we have come to regard as the natural concomitants of cerebral hemorrhage after forty years of age and a very large proportion of all cases present this picture

It is of interest to note that cardiovascular accidents are particularly liable to cause death or disablement in certain families owing to the early advent of degenerative changes in the cardiac valves the coronary and cerebral arteries and in the kidneys Any condition which weakens the arterial wall favors hemorrhage in the presence of a high blood pressure and it is still uncertain as to how frequently the escape of blood occurs from an aneurysm

Investigations seem to show that miliary aneurysms or minute dilatations of the smaller arteries are present in a large proportion of cases of cerebral hemorrhage and that these may be associated with larger sometimes dissecting aneurysms from which the fatal extravasation has taken place

Morbid Anatomy

Cerebral Softening —Encephalomalacia results in any part of the brain the arterial blood supply of which has been obstructed either by thrombosis or embolism (Fig 2) This ischemic softening is limited to the area supplied by the artery and resembles in most respects the infarcts of other organs produced by similar conditions

The changes produced by ischemia should be studied after the organ has been hardened as a whole since those of recent origin are liable to escape

detection if the brain is cut up on the post mortem table. They vary considerably with the age of the lesion.

In recent cases the ischemic area is swollen by serous exudation and, if it reaches the surface, the convolutions involved are enlarged and flattened. The consistence is little altered at first, but within a few days the central parts may be reduced to the consistence of creamy milk, which they resemble

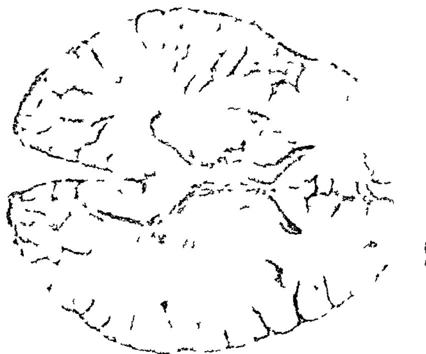


Fig. —Section of brain showing areas of softening in both hemispheres caused by gummatous arteritis of both middle cerebral arteries

also in color. The edges present a redder tint due to the escape of capillary blood into the softened tissue.

At a later period the softened area shrinks, the convolutions assume the appearance of moist wash leather and it is impossible to peel the soft meninges from their surface without tearing away portions of the disintegrated brain matter. When the destruction has not been complete the convolutions may retain much of their normal size, but their surface is somewhat hard and pitted, resembling that of beaten silver. On the other hand, when

large areas have undergone complete necrosis they are represented by cystic cavities containing clear or slightly turbid fluid (Fig 3) These cysts when they reach the surface and are covered by the pia arachnoid present the picture of porencephaly

In cases of advanced and general cerebral arteriosclerosis in which the whole brain has suffered severely from vascular malnutrition there may be seen not one area of ischemic necrosis but a large number of lacunar



Fig 3 — A brain showing the various results of cerebral thrombosis Note the porencephalic cavity the atrophied convolutions and the pitted surface of other sclerosed convolutions

softenings small fluid containing spaces with well-defined walls scattered throughout the hemispheres (Fig 4) This condition is associated clinically with progressive double hemiplegia

Sections taken from the ischemic area of a very recent case may be remarkable only for the coagulated blood contained in the distended blood vessel but this is usually associated with some impairment of the reaction of the tissues to staining reagents The nuclei are paler than normal and the myelin fails to stain well by the Weigert Pal method Nerve cell

quickly undergo degenerative changes and staining methods no longer bring out their characteristic appearance

Within a few days the microscopic picture is profoundly altered by the presence of large numbers of compound granular cells containing one or more nuclei and a protoplasm filled with fat droplets the products of tissue degeneration They are derived from the neuroglia or from



Fig 4.—Section of a brain with widespread atheroma of the arteries Thrombosis of the posterior cerebral artery has destroyed much of the left occipital lobe Small areas of softening are to be seen in the basal ganglia

fibroblasts and act as scavengers carrying their burden to the lymph spaces surrounding the blood vessel

The more highly specialized nerve elements succumb more easily than the neuroglia When necrosis is present the neuroglia is destroyed in the central parts of the softened area but in the peripheral parts neuroglia reaction may be detected This takes the form of an increase in the size of the cells division and multiplication of their nuclei and a proliferation of their processes These fibrils form a dense network which spreads inward and more or less fills up the space left by the destruction of brain matter

In smaller patches of softening the neuroglia survives and by its proliferation forms a sclerotic scar tissue which to some extent maintains the shape and size of the affected area. The blood vessels and their adventitial sheaths present a greater resistance to the necrotic process. Some are involved in the general disintegration but others remain as strands of connective tissue which take a share in the scar formation. Newly formed vessels and fibro-



FIG. 5.—Section of a brain showing a hemorrhage in the lenticular region.

blasts are found in the older lesions so that the margin of the necrosed area is often largely composed of young granulation tissue.

Secondary degeneration of nervous paths is the natural consequence of ischemic softening and the distant cells of the destroyed axones undergo "degeneration en distance." In the case of internal capsular lesions the Betz cells of the motor cortex are found to be reduced in number and those which survive to have undergone chromolytic changes.

Hemorrhage.—Hemorrhage from a diseased artery is more common inside the brain than on the surface and most frequent in the gray matter of the basal ganglia (Fig. 5). In this region are found the lenticulo optic and lenticulo striate arteries, to one of which Charcot gave the name of "the artery of cerebral hemorrhage."

Any cerebral artery may rupture and the consequent extravasation of blood may attain any size or shape. In severe cases the blood ploughs through the brain substance to reach the subarachnoid space or one of the ventricles. In the latter case it may fill one ventricle after another and reach the subarachnoid cistern in the posterior fossa of the skull and thence pass along the posterior surface of the spinal cord (Fig. 6).



Fig. 6.—Hemorrhage into the subarachnoid space at the base of the brain and spreading down the surface of the spinal cord.

In the case of small hemorrhages the blood pushes back the surrounding tissues and produces its interference with function by pressure and secondary edema rather than by actual destruction of nerve elements.

On the post mortem table the hemisphere which contains a large extravasation of blood is increased in volume and its convolutions are flattened and often anemic. In recent cases the hemorrhage is represented by a red clot which can be separated readily from the surrounding brain matter. The latter is broken and discolored while smaller capillary extravasations are often to be seen in the neighborhood. An edematous swelling of the surrounding tissues can usually be detected.

In somewhat older cases the clot is found to be shrunken and to be partly

In smaller patches of softening the neuroglia survives and by its proliferation forms a sclerotic scar tissue which to some extent maintains the shape and size of the affected area. The blood vessels and their adventitial sheaths present a greater resistance to the necrotic process. Some are involved in the general disintegration but others remain as strands of connective tissue which take a share in the scar formation. Newly formed vessels and fibro-



FIG. 5.—Section of a brain showing a hemorrhage in the lenticular region.

blasts are found in the older lesions so that the margin of the necrosed area is often largely composed of young granulation tissue.

Secondary degeneration of nervous paths is the natural consequence of ischemic softening and the distant cells of the destroyed axones undergo "degeneration en distance." In the case of internal capsular lesions the Betz cells of the motor cortex are found to be reduced in number and those which survive to have undergone chromolytic changes.

Hemorrhage.—Hemorrhage from a diseased artery is more common inside the brain than on the surface and most frequent in the gray matter of the basal ganglia (Fig. 5). In this region are found the lenticulo optic and lenticulo striate arteries, to one of which Charcot gave the name of "the artery of cerebral hemorrhage."

bosis and hemorrhage are in many respects similar at any rate as far as the presence of arterial disease is common to both

In discussing the etiology we have observed that arterial disease is present in most cases of cerebral hemorrhage and cerebral thrombosis the other factor of importance being the condition of the blood pressure In any particular case of apoplexy seen by a medical man within a few hours of onset it may be very difficult to determine whether the blood pressure was high or low when the stroke occurred and a decision on this point may be arrived at only from circumstantial evidence The shock produced by a severe hemorrhage may be associated with a temporary but considerable fall of blood pressure and the medical attendant may thus be deceived when he sees the patient at that stage

When a hemiplegia develops slowly in the course of a few hours perhap with remissions and relapses the diagnosis may again be a matter of some difficulty and the observer may have to decide whether the process is a slowly spreading thrombosis or a slow leakage of blood from a small vessel We have already seen that in both cases the disturbance of function may be complicated by edema of the tissues in the neighborhood of the lesion

In a typical case of cerebral hemorrhage the onset may occur when the patient is enjoying the best of health or if he has any premonitory symptoms they are those which are commonly associated with arteriosclerosis and a high blood pressure, such as occasional headaches and slight attacks of giddiness The seizure is abrupt and the patient may fall unconscious while engaged in some active physical pursuit or when under the influence of some violent emotion Death may be the immediate result but in the majority of cases the patient lies in a state of profound unconsciousness with slow and stertorous breathing The face is pale or slightly cyanosed and the skin is moist with sweat The eyes are only partially closed the pupils are contracted and react sluggishly to light The conjunctival reflex is either abolished or much diminished especially on the paralyzed side There is no reaction to painful stimuli the limbs are flaccid and the sphincters are relaxed Occasionally at this stage there are convulsive movements affecting the face and limbs on the side opposite to the lesion and in the interval between these movements the eyes may be persistently directed towards the non paralyzed side of the body All reflex movements are temporarily abolished or greatly diminished in activity

For a time it may be difficult to determine on which side of the brain the hemorrhage has occurred and only a careful examination enables the observer to come to a decision on this point The muscular tone detected while making passive movements of the limbs may be more completely lost on the hemiplegic side and the paralyzed side of the face may flap more obviously during respiration Some degree of response to painful stimulation may be

or altogether yellowish in color At a still later stage the site of the hemorrhage may be occupied by scar tissue or by a straw colored fluid The adjacent brain substance undergoes changes similar to those described as occurring around an area of necrosis an attempt to form scar tissue on the part of the neuroglial and connective tissues In fact it is often impossible to distinguish the remains of an old softening from those of an equally old hemorrhage in the brain of patients who have survived one of these vascular accidents for a considerable period of time Even under the microscope the changes are very similar except that the center of the focus in the case of hemorrhage is occupied by coagulated blood and not by necrotic brain tissue The clot produces the effects of a foreign body on the surrounding structures rendering them anemic and edematous The nerve cells undergo regressive changes the axones become swollen and varicose and the myelin sheaths break up into fatty droplets Compound granular cells rapidly make their appearance and carry on the scavenging work for which they are destined Ultimately the altered clot is invaded by spindle shaped cells with large vesicular nuclei and by new blood vessel forming a granulation tissue which tends with more or less success dependent on the original size of the hemorrhage to obliterate the defect in the structure of the brain Secondary degeneration of the nervous tracts involved in the hemorrhage may be traced by means of the Marchi or Weigert Pal methods of staining

Symptomatology of Vascular Hemiplegia

Hemiplegia or paralysis of one side of the body is only one of the many disturbances of function which can be and are produced by vascular accidents in the brain It is the frequency with which the middle cerebral artery and particularly those branches which supply the internal capsule and surrounding structures is involved which makes a stroke or apoplexy of such common occurrence as to deserve separate consideration

Hemiplegia is a symptom not a disease and the clinical features by which it is characterized are the same whether the lesion responsible for it is vascular inflammatory neoplastic or degenerative The vascular hemiplegias moreover are the same whether they result from softening or from hemorrhage and the only part of the clinical picture which may present differences is the mode of onset Before discussing the various modes of onset it may be as well to state that in a large number of cases it is difficult to determine whether the lesion is in the nature of a thrombosis or a hemorrhage although it is quite clear that the condition is of vascular origin This should not cause much surprise in view of the fact that the conditions favoring throm

apparently good health Convulsive movements affecting the whole or part of the paralyzed side may recur from time to time during the development of this condition

Premonitory symptoms of thrombosis take the form of transient sensations of formication or numbness in one or other limb or in the case of left sided lesions of transient attacks of difficulty in speech or aphasia These premonitions may recur from time to time over a period of weeks or even months especially in old people with enfeebled hearts and are indicative of transient ischemia in parts of the cerebral circulation

The Signs of Hemiplegia

These are the result of a lesion of the corticospinal tract and differences depend only on the extent and not on the nature of the damage inflicted by the vascular accident There are certain principles which should always be remembered in relation to the effects produced by unilateral interference with the functions of the pyramidal tract In the first place it should be realized that movements not muscles are affected In the second place the movements most affected are those which are naturally unilateral In the third place the more highly specialized movements those which have been latest developed are more affected than those which are completely or nearly completely automatic In a hemiplegic patient after the shock stage has passed away the affected side of the face may exhibit little change at rest although there may be differences in the lines of the face Little asymmetry may be observed during strong emotional movements but voluntary actions such as that of showing the teeth bring out the weakness on the affected side Closure of the eyes may be well performed but if resistance is offered the strength of the closure movement on the affected side can be demonstrated moreover the patient is unable to close the eye on that side without closing the other at the same time Movements of the forehead and eyebrows being largely bilateral are little affected The functions of phonation articulation mastication and deglutition being largely automatic and bilateral are not interfered with to any extent and the tongue performs its ordinary movements with little difficulty If the patient is asked to protrude his tongue it tends to deviate towards the side of the lesion

The movements carried out by the muscles of the neck and the trunk which are largely concerned in the automatic maintenance of the erect position are comparatively little affected compared with those of the limbs Hughlings Jackson pointed out that in automatic respiration the movements of the affected side of the chest may be slightly greater than those of the opposite side but when a forced respiratory effort is made the asymmetry is reversed

obtained on the non paralyzed side and sometimes an extensor response is only obtained from the opposite foot

This condition of coma may persist for hours and even days and death may take place at any period In non fatal cases recovery from the comatose condition is gradual and is indicated in the first instance by signs of irrita bility and resentment in answer to manipulations and examinations Any pinching of the skin produces a defensive movement especially on the non paralyzed side The patient resents light thrown into his eyes and the conjunctival reflex returns on the side of the lesion Within a few hours there is generally a slight rise of temperature which is more marked on the par alyzed side Ophthalmoscopic examination during the comatose stage may reveal no abnormalities but in a considerable proportion of cases there is some edema of the discs which may be associated with retinal changes characteristic of renal disease

In other less severe cases of cerebral hemorrhage the patient may suffer from momentary loss of consciousness or from transient giddiness associated with loss of power in the limbs on one side This condition of hemiplegia may pass away in a few hours or a few days perhaps to return in a more severe form if the warning it provides has not been attended to

In cases of cerebral softening due to embolism the onset is always abrupt it is often accompanied by loss of consciousness and sometimes by convul sions When the area of brain involved is a small one consciousness may be retained and the patient may only complain of pain in the head and giddiness or faintness while the hemiplegia develops

The symptoms of hemiplegia resulting from thrombosis of the cerebral arteries may be either abrupt or gradual in onset In the former case they can hardly be distinguished from those of cerebral hemorrhage and the diagnosis must depend upon any data which may be available in regard to the condition of the patient s health and blood pressure More commonly thrombosis is manifested by a very insidious onset of hemiplegia The patient on attempting to leave his bed in the morning finds that he is unable to stand or he may be sitting quietly in a chair and finds that one or other hand has become weak or powerless He may be quite free from any signs of discomfort in his head and is apt to regard the uselessness of an arm as the result of its having been rested in some unaccustomed position for an undue length of time He may not realize that the leg on the same side is affected until he attempts to get up and move away Not infrequently the loss of power passes off in the course of a few minutes only to return in a more permanent form some hours later

Another mode of onset is characterized by the slow development of hemiplegia followed by loss of consciousness and in many cases the patient is found in this condition in the morning after having gone to bed at night in

passive position and passive movement is generally affected for a long time and in many cases permanently

Crossed Hemiplegia

When a vascular lesion affects the corpus quadrigeminal region there may be found third nerve palsy on one side associated with paralysis of the face arm and leg of the opposite side Vascular lesions in the pons due to hemorrhage or thrombosis of one of the branches of the basilar artery produce another form of crossed hemiplegia in which the face may be affected on one side and the arm and leg on the other side Under these circumstance the facial palsy may show the characteristic features of a nuclear lesion All the facial muscles may be involved and may undergo atrophy and the electrical reaction of degeneration

Double Hemiplegia

This occurs as the result of vascular accidents either from a single lesion in the pons where the two pyramidal tracts are in close approximation or from two separate lesions occurring at different times in the internal capsules of both hemispheres The picture presented in either case is that to which the term pseudobulbar palsy has been given In double hemiplegia we find not only all the signs associated with hemiplegia on both sides of the body but in addition an interference with a number of other functions which escape when the lesion is unilateral Thus articulation and deglutition become involved and the patient suffers from dysarthria and dysphagia His powers of mastication may be seriously affected and his trunk movements may be so enfeebled as to add greatly to his general disability In these cases too there is usually much impairment of sphincter control

Trophic Disturbances

Bedsores are not a common complication of the hemiplegic state but may occur in the early comatose stage following a cerebral hemorrhage or thrombosis unless very careful nursing is carried out General loss of weight is likely to occur in the early stages but may be followed by an increase due to the interference with activity Atrophy of muscles on the paralyzed side is usually inconspicuous but in certain cases it is remarkable even in the absence of arthritic changes Secondary arthritis is common especially in the shoulder joints but depends very largely on the amount of attention and treatment which is given to the limbs while the patient is bedridden

Vasomotor disturbances are common and the affected limbs are usually

In the majority of cases of hemiplegia the arm is more affected than the leg and the movements of the fingers more affected than those at the shoulder, elbow and wrist. After a preliminary stage of flaccidity there is a tendency for the limb to adopt a definite posture which is determined by involuntary adduction and internal rotation at the shoulder, flexion and pronation at the elbow and flexion of the wrist and fingers. The last movements to be regained are the finer and more specialized functions of the thumb and finger, and it is rare that the patient who has sustained a severe attack of hemiplegia is able to carry out such delicate manipulations of the hand as are involved in playing instruments with his previous facility.

The lower extremity assumes a position of extension with the foot in the position of equino varus. Walking is made difficult by the toes catching the ground, and the patient learns to overcome this obstacle by circumducting the leg at the hip when he advances the limb.

Associated with these limb postures is found an increase of tone or rigidity in the muscles which preponderate and any attempt to passively correct the postures is met by a certain amount of involuntary resistance. In the course of time the affected muscles and tendons become contracted and the postures thus become permanent deformities.

It is characteristic of hemiplegia that certain automatic acts are associated with involuntary movements. Thus a patient may be unable to extend his fingers and wrist voluntarily but may perform those movements involuntarily while yawning. Another remarkable feature is the tendency for the paralyzed limbs to make movements in association with strong muscular movements carried out on the non paralyzed side.

All tendon jerks in the paralyzed limbs are increased and clonus may be elicited in certain situations, such as the knee and ankle, more rarely in the upper extremity. On the paralyzed side the abdominal and cremasteric reflexes are usually abolished except in young children and the plantar reflex is altered in character. On stimulating the sole of the foot the big toe is extended instead of flexed. Disturbances of the sphincter reflexes do not as a rule persist for long after the initial stage, but the patient may complain of some precipitancy in connection with the bladder.

The above description applies to the majority of cases of hemiplegia but there are exceptions to the general rule in regard to the question of rigidity and posture. In some cases, for instance, the tone is not increased and the limbs may remain flaccid even when a certain amount of recovery of voluntary movement has been obtained. This is particularly the case when the motor loss is complicated by considerable disturbances of sensibility. In ordinary cases of hemiplegia the hemianesthesia which may be present in the early stages tends to disappear, at any rate as far as sensibility to painful and thermal stimuli is concerned. On the other hand the sense of

tinguish between cases of cerebral hemorrhage and cases of uremia and it must be remembered (a) that a cerebral hemorrhage may precipitate the onset of uremic coma in a patient suffering from renal disease (b) that a patient suffering from granular kidney is particularly prone to cerebral hemorrhage and (c) that in uremia hemiplegic signs and symptoms are apt to arise even in the absence of a cerebral hemorrhage

Hemiplegia is a not uncommon result of encephalitis but in these cases it is usually associated with or preceded by other symptoms in the form of headache pyrexia ocular palsies etc It should not be forgotten however that a cerebral hemorrhage may occur as a complication of encephalitis and in some cases an examination of the cerebrospinal fluid may afford a clue to the diagnosis Hemiplegia may be present in the congestive attacks of general paralysis of the insane but is usually transitory and signs of syphilis can be detected

2 The diagnosis of cerebral embolism is dependent on the presence of some condition favoring the production of an embolus in the thoracic organs *It can hardly be made unless evidence of old or recent endocarditis is present* Cerebral hemorrhage can be presumed as the cause of hemiplegia in the case of a patient who has a high blood pressure a full bounding pulse and a hypertrophied left ventricle but cannot be excluded within a few hours of the stroke if the blood pressure is then low and the heart s action rapid and feeble as the result of shock Cerebral thrombosis is the usual cause of a hemiplegia which develops slowly in the course of a few hours in elderly people with enfeebled circulation On the other hand there is little doubt that cerebral hemorrhage is sometimes a secondary result of cerebral softening and occurs in relation to a vessel which has lost the natural support afforded by healthy surrounding tissues

Speaking generally there are many cases in which the diagnosis between thrombosis and hemorrhage is impossible especially if it is attempted at a considerable distance of time after the stroke has occurred

PROGNOSIS

An attempt to prophesy what is going to take place in the case of a vascular hemiplegia is more or less a matter of guess work It is impossible to determine by any methods at our disposal whether the interference with the function of the pyramidal tract in the early stages is due to an actual destruction of the fibers or to pressure and edema secondary to a lesion in their neighborhood In the former case regeneration is impossible and the hemiplegia must therefore be permanent In the latter case a complete recovery is not only possible but probable In the majority of instances

cyanotic and sometimes edematous especially in their peripheral parts Sweating may be excessive but the surface temperature is generally reduced to the extent of several degrees as compared with the sound side

Involuntary Movements

In a small proportion of cases of hemiplegia there is observed a variety of involuntary movements Sometimes there is a fine rhythmical tremor not unlike that of paralysis agitans Other cases exhibit a tremor of the so-called intention type most marked at the termination of a purposive movement Following the infantile hemiplegias athetotic and choreiform movements present a distressing complication and once established they tend to persist indefinitely

Pain in Hemiplegia

In the majority of cases of vascular hemiplegia pain is not a conspicuous symptom and when complained of can generally be referred to arthritis This occurs when the paralyzed limbs have been allowed to remain in fixed positions and passive movements have been neglected There are however occasionally seen cases of hemiplegia associated with what is known as the thalamic syndrome These patients present peculiar sensory disturbances Their appreciation of painful and thermal stimuli is lowered but such stimuli when sufficiently strong produce intensely disagreeable results which are badly localized In addition these patients frequently complain of severe paroxysms of pain referred to the paralyzed limbs

DIAGNOSIS OF VASCULAR HEMIPLEGIA

The diagnosis of vascular hemiplegia can be conveniently divided into two parts (1) The differentiation of apoplexy from other conditions giving rise to acute and profound loss of consciousness (2) The diagnosis between cerebral hemorrhage cerebral thrombosis and cerebral embolism

1 A state of apoplexy may be mistaken for an acute toxic condition such as is produced by alcohol opium or diabetic coma The presence therefore of asymmetrical hemiplegic signs on careful investigation should prevent this mistake being made An alcoholic odor should not be deemed a strong point in favor of alcoholic poisoning as the taking of alcohol is a not infrequent precursor of hemorrhage An early examination of the urine should always be made in these states and this should be sufficient for the detection of diabetes The presence of albuminuria does not suffice to dis

In order to avoid this an attempt may be made to tap the clot and drain it through an artificial opening chosen by the operator. Ligation of the carotid artery on the side of the hemorrhage has been performed in a certain number of cases but this operation is attended by the risk of causing widespread softening and can rarely be justified.

When the acute stage has passed and the patient is recovering consciousness the chief symptom to be met is that of restlessness. A simple sedative like bromide combined with complete quiet may be a sufficient remedy but morphia may be necessary and beneficial. Rest in bed for a few weeks with careful nursing and a low diet should be ordered in every case.

Cerebral Thrombosis

In the acute stage the patient should be kept absolutely still as in the case of cerebral hemorrhage. If the patient is suffering from a weak heart and a low blood pressure active purgation must be avoided and the bowels kept open by means of a mild aperient and enemata. Feeding either by the mouth or by the rectum should be commenced at an early stage and stimulation by means of alcohol and digitalis may be indicated. If syphilis is suspected an intramuscular injection of mercury may be given at once and repeated at weekly intervals or the same effects may be attained by means of daily inunctions. Potassium iodide in increasing doses should be administered by the mouth as soon as the patient is able to swallow.

Hemiplegia

It has already been pointed out that in all vascular accidents affecting the brain it is impossible to determine how far the symptoms are due to destruction of nerve tracts and how far they are the result of edema and compression. This ignorance justifies the adoption of a hopeful attitude and necessitates the employment of every measure likely to facilitate recovery even in the most unpromising cases.

Success in dealing with hemiplegia depends largely on an intelligent anticipation of the difficulties which are likely to be met with and on enlisting the patient's active cooperation in his treatment.

Armed with the knowledge that the patient's paralyzed limbs will tend if uninterfered with to assume certain fixed positions already described it should be the object of the doctor and nurse to counteract this tendency from the beginning. Even during the comatose stage the nurse should see that the arm and leg particularly the former are never allowed to lie for long periods in one position. The upper arm should be kept away from the chest by an interposed pillow the forearm should often be supinated and placed

there may be a combination of both factors at work so that the result is a partial recovery of function Speaking generally the less severe the initial lesion the less prolonged the state of coma if such exists the better the prognosis but a primitive knowledge of the anatomical conditions makes it quite clear that even a small lesion may produce permanent results It is generally safe to say that some recovery is likely to take place but that time alone can show to what extent function can be regained

Treatment

Cerebral Hemorrhage

A patient suffering from apoplexy or from any symptoms even suggestive of an approaching seizure should be put to bed without delay and kept there If there is reason to suppose that hemorrhage is occurring precautions should be taken to avoid all unnecessary movements and all mental and physical disturbances

The comatose patient should lie with his head and shoulders slightly raised and the face turned to one side in order to prevent the tongue falling back and so interfering with respiration If a water bed is available it should be used but it is unwise to shift a patient during the first few hours for this purpose The bladder should be emptied by means of a catheter and the patient kept clean and dry with scrupulous care Starvation for twenty four hours will probably be beneficial but the patient s mouth should be kept clean by frequent sponging and the use of some antiseptic preparation such as boro glyceride The action of the bowels should be obtained as soon as possible by the administration of calomel or croton oil followed if necessary by an enema

In the case of patients with a high blood pressure and obvious signs of congestion the question of bleeding has to be considered No dogmatic opinion can be given on the efficacy of this measure but it may be assumed that no harm will result from the removal of 10 to 20 ounces (300 to 600 c c) of blood by venesection The number of cases in which bleeding can be stated with confidence to have saved the patient s life must be very small

Still more caution is required in considering the employment of surgical decompression as a therapeutical measure in these cases When a patient s life is threatened by increased intracranial pressure it may be justifiable to perform a subtemporal decompression both the bone and dura being freely opened This operation is not without the risk of producing an increased amount of laceration of brain substance as the extravasated blood may burst through the convolutions on to the surface of the unsupported area of brain

In order to avoid this an attempt may be made to tap the clot and drain it through an artificial opening chosen by the operator. Ligation of the carotid artery on the side of the hemorrhage has been performed in a certain number of cases but this operation is attended by the risk of causing widespread softening and can rarely be justified.

When the acute stage has passed and the patient is recovering consciousness the chief symptom to be met is that of restlessness. A simple sedative like bromide combined with complete quiet may be a sufficient remedy but morphia may be necessary and beneficial. Rest in bed for a few weeks with careful nursing and a low diet should be ordered in every case.

Cerebral Thrombosis

In the acute stage the patient should be kept absolutely still as in the case of cerebral hemorrhage. If the patient is suffering from a weak heart and a low blood pressure active purgation must be avoided and the bowels kept open by means of a mild aperient and enemata. Feeding either by the mouth or by the rectum should be commenced at an early stage and stimulation by means of alcohol and digitalis may be indicated. If syphilis is suspected an intramuscular injection of mercury may be given at once and repeated at weekly intervals or the same effects may be attained by means of daily inunctions. Potassium iodide in increasing doses should be administered by the mouth as soon as the patient is able to swallow.

Hemiplegia

It has already been pointed out that in all vascular accidents affecting the brain it is impossible to determine how far the symptoms are due to destruction of nerve tracts and how far they are the result of edema and compression. This ignorance justifies the adoption of a hopeful attitude and necessitates the employment of every measure likely to facilitate recovery even in the most unpromising cases.

Success in dealing with hemiplegia depends largely on an intelligent anticipation of the difficulties which are likely to be met with and on enlisting the patient's active cooperation in his treatment.

Armed with the knowledge that the patient's paralyzed limbs will tend if uninterfered with to assume certain fixed positions already described it should be the object of the doctor and nurse to counteract this tendency from the beginning. Even during the comatose stage the nurse should see that the arm and leg particularly the former are never allowed to lie for long periods in one position. The upper arm should be kept away from the chest by an interposed pillow the forearm should often be supinated and placed

in the extended position and the wrist and fingers may even be placed for a few hours at a time in some form of splint to oppose continued flexion Passive movements should be carried out at least two or three times daily at every joint and gentle massage applied to the muscles

As soon as the patient recovers consciousness and is sufficiently recovered mentally to appreciate his condition he should be educated up to the belief that he is going to take the chief part in his own treatment He should be told that his arm and his leg are not the seats of his disease that every voluntary movement will require his own initiation and that the manipulations of the nurse and the masseur aim only at keeping the limbs in good condition It is equally important that the masseur should appreciate his own limitations and that he should encourage the patient to cooperate in all movements The patient will naturally tend to practise and strengthen those movements which come first and most easily to him He should be instructed not to neglect those he finds difficult or even those he cannot perform It is a good plan to explain to him the different movements which are naturally performed at each joint and to ask him to spend a certain amount of time every day attempting each movement in turn even in the absence of any physical response He should do the same thing while the masseur is carrying out passive movements and the latter should engage his attention to this end

Only by such methods will the patient overcome the resistance offered to his recovery in the form of spasticity contractures and deformities and only by steady perseverance in them will he obtain the maximal amount of voluntary power which is possible in his case Equally important is the avoidance of bad habits when the patient begins to get about If left to himself the patient will walk with an extended leg which he circumducts and swings in order to prevent the toes catching the ground He should be taught to persevere in advancing his leg by flexion at the hip and knee, and he should not be allowed to sit with his paralyzed leg adducted and his toes pointing inwards

It will be noticed that no mention has been made of electrical treatment in regard to these cases Electricity has no place in the treatment of hemiplegia and its daily application to the paralyzed limbs is a waste of time and money in the large majority of cases It tends to make the patient believe that recovery is going to take place as the result of external applications and so minimizes the value of his own efforts which are all important It can only be of use in rare cases in which certain muscles have undergone secondary atrophy

The principles which should govern the treatment of hemiplegic patients having been grasped, the medical attendant will be able to apply them and modify them in relation to individual cases

CHAPTER II-A

CEREBRAL ARTERIOSCLEROSIS WITH REPEATED THROMBOSIS OF SMALL INTRACRANIAL ARTERIES

By WALTER C. ALVAREZ

TABLE OF CONTENTS

INTRODUCTION

Synonyms — Spasm of intracranial blood vessels minor apoplexies small strokes vascular accidents

Definition — Cerebral arteriosclero is is a chronic disease of the small intra cranial arteries which results in thrombosis here and there and the formation of many infarcts most of them less than 5 mm in diameter With each infarct a small part of the brain is destroyed and eventually enough is put out of action so that the victim becomes tired and weak perhaps changed in character and aged beyond his years In the end the process results in death perhaps 10 15 or 20 years after the first symptoms appear

As will be seen later many of the infarcts are too small to produce any recognizable symptoms larger ones may result in dizziness a sense of great fatigue a loss of the feeling of well being loss of interests loss of memory or a loss of ability

in the extended position and the wrist and fingers may even be placed for a few hours at a time in some form of splint to oppose continued flexion Passive movements should be carried out at least two or three times daily at every joint and gentle massage applied to the muscles

As soon as the patient recovers consciousness and is sufficiently recovered mentally to appreciate his condition he should be educated up to the belief that he is going to take the chief part in his own treatment He should be told that his arm and his leg are not the seats of his disease that every voluntary movement will require his own initiation and that the manipulations of the nurse and the masseur aim only at keeping the limbs in good condition It is equally important that the masseur should appreciate his own limitations and that he should encourage the patient to cooperate in all movements The patient will naturally tend to practise and strengthen those movements which come first and most easily to him He should be instructed not to neglect those he finds difficult or even those he cannot perform It is a good plan to explain to him the different movements which are naturally performed at each joint and to ask him to spend a certain amount of time every day attempting each movement in turn even in the absence of any physical response He should do the same thing while the masseur is carrying out passive movements and the latter should engage his attention to this end

Only by such methods will the patient overcome the resistance offered to his recovery in the form of spasticity contractures and deformities and only by steady perseverance in them will he obtain the maximal amount of voluntary power which is possible in his case Equally important is the avoidance of bad habits when the patient begins to get about If left to himself the patient will walk with an extended leg which he circumducts and swings in order to prevent the toes catching the ground He should be taught to persevere in advancing his leg by flexion at the hip and knee and he should not be allowed to sit with his paralyzed leg adducted and his toes pointing inwards

It will be noticed that no mention has been made of electrical treatment in regard to these cases Electricity has no place in the treatment of hemiplegia and its daily application to the paralyzed limbs is a waste of time and money in the large majority of cases It tends to make the patient believe that recovery is going to take place as the result of external applications and so minimizes the value of his own efforts which are all important It can only be of use in rare cases in which certain muscles have undergone secondary atrophy

The principles which should govern the treatment of hemiplegic patients having been grasped the medical attendant will be able to apply them and modify them in relation to individual cases

facts to the attending physicians They talk only of the digestive disturbances

Oftentimes the family physician will promptly make the correct diagnosis because he knew the patient before the acute episode and he can see the tremendous change that came suddenly at a certain minute of a certain day He perhaps goes into the home and sees what a terrible problem is being faced by the family and he may also hear from the man s business associates that at the office he is no longer of any use he is no longer initiating anything and he is perhaps so irritable and unreasonable that he is fighting with all his subordinates

The problem of diagnosis is much more difficult for the city consultant because he never saw the man before and hence does not know what sort of person he was He seldom gets the story of the initial stroke he seldom learns of the terrible problem in the patient s home and he seldom hears about what is happening at the man s place of business As already noted neither the patient nor the family mentions the really significant parts of the history and hence if the consultant does not note signs of mental deterioration or get a hunch as to what happened so that he thinks to ask the relatives about a sudden illness with a change in character and efficiency he will miss the correct diagnosis If as is so customary today he depends for his diagnosis on the results of laboratory tests and roentgenological studies of the digestive tract he will be led astray because the tests will not help him

One sweet old lady summed up the situation very well when she said death is taking little bites of me She saw that with each attack of dizziness or fainting or mental confusion she became a little older a little weaker and a bit more tired her step became more hesitant her memory less trustworthy her handwriting less legible and her interests in life less keen She could see clearly that for 10 years or more she had been moving step by step toward the grave

The only physician who saw this problem in its entirety appears to have been Osler who in his usual inimitable way spoke of the many men and women who take as long to die as they did to grow up who go through cold gradations of decay and who live a sort of death in life

Distribution and Occurrence

This disease probably begins most often in the fifties and sixties but not infrequently it begins in the forties and there is considerable evidence to indicate that in some persons it begins in the thirties Naturally when a sudden dizzy spell followed by a nervous breakdown comes in the thirties or forties it is hard to say if it was part of the disease which eventually killed the patient in the fifties or sixties but there are many case histories which suggest strongly that this was the case Every physician of experience knows that vascular accidents with

to work Naturally the severity of the symptoms depends on the extent and number of the infarcts and their location in the brain

The patients commonly live on for years without becoming demented or childish or without the nature of their disease becoming apparent Only occasionally will an infarct be large enough or so situated in the brain that the attending physician can see clearly that an injury was wrought to the nervous system Many a person with this disease has one or more episodes and then goes for years without another recognizable one

History

A search through the literature so far has not revealed any good description of this common disease A few outstanding clinicians like Janeway and Peabody mentioned it but curiously appeared to be reluctant to go ahead and describe it in detail Because the manifestations of the malady are usually spread over 10 or 20 years and the several episodes are seen by different physicians few internists have a chance to learn anything about the disease in its entirety About the only way in which a physician can come to know this disease well from start to finish and with all its bizarre manifestations is to watch a parent or close relative or friend die slowly from it For some strange reason the disease is seldom mentioned in books or journals it practically never is discussed at medical meetings and perhaps never is a case demonstrated before medical students in the college amphitheater

In books on arteriosclerosis psychiatry neurology or geriatrics one can find descriptions of the types of senile dementia which can result from a severe apoplexy or a series of them but one seldom finds descriptions of the type of mild episode described here and nowhere has the writer found a detailed description of the long lasting episodal disease dealt with in this article

One big reason for this is that physicians have a strong repugnance for making the diagnosis of a stroke They fear to discourage and to offend or to cast a stigma on the patient and the family and hence in these cases they usually diagnose acute indigestion or Meniere s disease or a liver attack or a heart attack In many cases it is only the patient and his family who recognize the fact that there was a little stroke, or they have a good hunch that this is what happened In all bad cases the wife and the family usually will realize that something terrible happened to the patient s brain they see perhaps a big change in character and personality, and often they have on their hands a changeling who is extremely difficult and trying to take care of Often he is worse than any problem child He is no longer the strong and efficient and friendly person he was before the cerebral accident Often the family realizes that the wage earner is done for and will never work again but curiously they seldom mention these



Fig 1 Results of thrombosis in many small arteries of the brain (from Alvarez)

tion showed little that was noteworthy the one significant finding probably was that he talked out of one side of his mouth The blood pressure was 140 mm Hg systolic Extensive laboratory tests and roentgenological examinations of the digestive tract failed to show any sign of disease Later during the course of three long interviews the following history was elicited with much difficulty

The man had enjoyed perfect health until 5 years before when on July 18 1930 at 10 30 in the morning there came a series of short severe stabbing pains in the upper part of the head He was much upset over this and never felt right again Another curious attack came 5 months later when a feeling of great lassitude flashed over him Two months later he woke with a head on him as if he had been drinking heavily the night before Actually he had not been drinking When a physician arrived he found an elevated blood pressure After that morning the patient never had a comfortable moment His bowels which had always moved perfectly before became constipated and he felt that this was affecting his mind and producing a miserable feeling in his head Largely for this reason he kept going to gastroenterologists At times he had burnings and quivering feelings in his legs and hand

During the next 4 years he saw many physicians in a vain search for health Various

typical hemiplegia can happen to young persons even in the second and third decades of life and during the last war it was noted that quite a few young soldiers suffered a coronary thrombosis

It is probable that thrombosis of small intracranial vessels occurs more commonly in persons with a tendency to hypertension, but in many cases there is no increase in pressure Good statistics are not yet available, but it seems probable that women are as subject to the disease as are men and perhaps more so There can be no question about the fact that a high percentage of persons are pulled down slowly and finally killed by this disease if only because at necropsies the pathologist finds the lesions so commonly

Etiology

Little is known about the etiology As already noted the presumption is that the little thrombi come because of sclerotic injuries to the small blood vessels of the brain The nature of many family histories suggests that there is a hereditary tendency to the disease Occasionally one will see families in which several of the members were wiped out early in life by either cerebral or coronary thrombosis

Pathology

Figures 1 to 5 show the common macroscopic lesions of the disease In a typical case the brain is speckled with little black spots showing where thrombosis took place With the microscope smaller brownish areas of atrophy can be seen A few larger areas of softening may also be found one of them perhaps representing the thrombosis that brought about the patient s death

It will be seen that the lesions are different from those of Pick s and Alzheimer s disease It will be seen also why with these many little areas of destruction in silent areas it is usually impossible for a neurologist to show weakness of any muscle or any abnormal reflex or anywhere a patch of anesthetic skin

Life History of the Disease

Doubtless the best way in which to show the life history of the disease and its long clinical course will be to describe a few cases

Case Records of Little Strokes

Case 1 — An engineer of 66 years secretary to a big corporation came complaining of intestinal discomforts for which for years he had been treated strenuously by gastroenterologists The story as told to the assistant who first saw the man was a vague one of indigestion colonic discomfort and feelings of auto intoxication Physical examina



Fig 3 Results of thrombosis of small arteries (from Alvarez)

traveling in dangerous places without ever a bit of fear he became so afraid of being alone that he insisted on his sister s coming to live with him

Soon after this the man s mental processes became so disorganized that he was unable to work It was no wonder that he told a rambling story and that it was difficult to get from him the really important detail

Case 2 — A stout woman aged 53 years in the menopause complained of attacks of epigastric pain and soreness in the abdomen This had been bothering her for 20 years but it had gotten worse in the previous 2 years There were occasional spells of nausea belching vomiting and diarrhea Food felt as if it were staying like a lump in the stomach

The woman had been examined roentgenologically many times and little wrong had ever been found For a time the systolic blood pressure had been more than 200 mm Hg Important was the fact that in the previous eighteen months without any change in her diet she had lost 30 pounds (13 6 kg) She felt miserable all the time with a great sense of fatigue

Examination showed only a tender abdominal wall and hypertension She was nervous and jumpy and the deep reflexes were exaggerated All the usual laboratory and roentgenological studies were negative



FIG 2 Results of thrombosis of medium and small arteries (from Alvarez)

diagnoses were made of colitis auto intoxication anxiety neurosis and hypochondriasis

The significant points in the history appeared to be (1) that a lifetime of good health was terminated on a certain hour of a certain day (2) that following the third sudden shock life became a burden and (3) that the disease kept growing worse in steplike stages As the man said every few months he had a little earthquake and with each one of these he became worse

Further questioning elicited the fact that after one of these earthquakes there was a tendency for the right leg to draw up and after another one his mouth filled with ropy saliva as it does sometimes with injuries to the brain stem Another one of his little strokes brought some hoarseness another brought dribbling of urine another made his walk unsteady Important was the testimony of the secretary who had been with him for years She noted that with the first shock he changed greatly his handwriting became bad his attention poor his memory deficient and the organization of his thoughts so poor that she had difficulty in taking a letter from him

A significant symptom was the man s fear of being left alone After a lifetime of

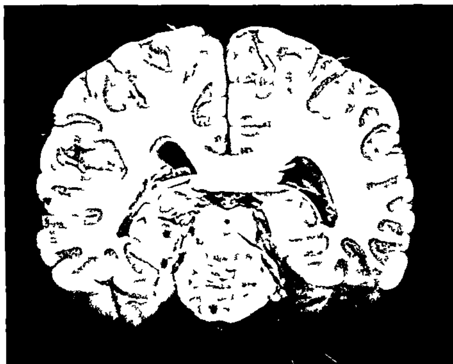


Fig 5 Results of thrombosis in small vessels

It was hard to say how much of this woman s abdominal distress was due to arteriosclerosis and the little injuries to her brain but certainly her illness as a whole was due to a long series of slight apoplexies One wonders also if the first spell at the age of 31 was due to the same disease process It is probable that it was One has to assume this because so many other patients with this disease tell a story of early attacks

This case illustrates the remarkable tendency patients with this disease have of complaining to the physician about everything but the little apoplexies This disease must be suspected and then the story must be dug out with great pertinacity

Case 3 — A college president during the latter half of his life was subject to nervous breakdowns The first came at about the age of 33 years and another 6 years later On each of these occasions the man had to take a year off to recuperate He would get tired and thin and unable to work and albumin would be found in his urine At the age of 45 he had another breakdown so severe that he had to resign from his position He was

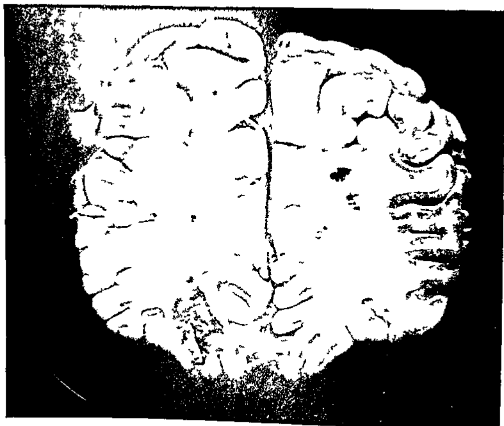


Fig 4 Results of thrombosis in small and medium vessels and hemorrhage from a small vessel (from Alvarez)

Finally after several long interviews the story was obtained that she began to have trouble 22 years before when at the age of 31 she suddenly felt her hands and arms go dead For a time this left some weakness so that she could not safely carry things Later some of this weakness cleared up but the deadness and discomfort in the arms remained A few years before she was seen by the writer she began to have curious spells of faintness She had to stop driving her car because on two occasions she lost consciousness After one of these spells the blood pressure dropped from the usual 200 to 135 mm Hg Then she had a spell in which she almost lost consciousness and after that she was weak and dizzy her handwriting became bad and for a time she could not talk clearly

After one of the spells she felt so queer that she went to a psychiatrist Then a coronary artery thrombosed and she had a little anginal distress Later in a spell she fell to the floor and was in coma for a day In another slight spell her face was pulled to the left and the right arm and leg were weakened Following this she was laid up for a month and had to use her left hand for eating and writing

thrombosis and necropsy showed the brain speckled with scores of little black and brown infarcts In addition there were a few larger areas of softening There were enough to account for all the dozens of little attacks which she had had No other lesion was found in her body to account for the long illness

In this case the woman kept until her last days most of her old personality her old interests her intelligence and understanding her good grooming her sweetness of disposition and her thoughtfulness for others about her She still remained sociable and liked to work a little around the house

Case 5 — An unusually able man always had had perfect health and driving energy until the age of 45 years He then suddenly found himself so weak and tired that every day he had to push himself to work Careful studies failed to show any sign of disease Months later because of abdominal discomfort a surgeon removed the appendix but this did not help and to a large extent the man had to retire from business A year or so later he had little attacks which were thought to be due to heart disease but the subsequent course of his disease suggested that they were more probably the result of paresthesia in the thorax due to thrombosis of small vessels in the brain These attacks wore him down until he had to quit work Fifteen years later he was still keen and friendly and well groomed and with many of his old interests in work and family He went to his office occasionally but could not do much Then his feet began to shuffle and he became afraid of being alone Later his face began to lose its expression and soon he had a typical Parkinson's syndrome In the next few years he got worse and wound up as a paralytic in bed His brain kept pretty clear until the end Death set him free 21 years after the disease began

Case 6 — A typical story of distress suddenly referred out from the brain into the abdomen was told by an able woman physician who one day when she was in her fifties suddenly felt as if something had been pulled in two in her abdomen There was some shock and for the next 6 weeks the woman lay in a hospital bed greatly distressed mentally and unable to sit up because of a feeling that her spine was gone Months later she had another similar episode which again put her to bed for weeks At no time was there any sign of injury to any abdominal organ There was no peritonitis and repeated roentgenological studies of the digestive tract showed nothing wrong At no time was there any serious trouble with digestion The patient gradually recovered and was well except for feelings of fatigue and poor health

The next case illustrates the way in which thrombosis of a small intracranial artery with a storm going down the vagus nerves can produce an overly irritable digestive tract with spasticity perhaps of the gastrointestinal muscle and exaggerated reflexes in the gut

Case 7 — A woman of 56 years who looked much older than that complained of spasmodic pain in the epigastrium and nausea which came the minute she put any food or even water into the stomach There was also weakness and loss of weight Even the effort of trying to eat wore her out Careful roentgenological studies of the digestive tract showed what was probably the scar of an old duodenal ulcer

Questioning the husband finally brought out the story that after a lifetime of perfect health the woman's trouble had all come 4 months before on a Tuesday about 7 30

thought then to have either Bright s disease or tuberculosis The course of events showed that he had neither disease but more probably an episode in the course of the cerebral arteriosclerosis which eventually killed him

After resting a year the man went to work again at an easier job Two years later he had a sudden severe shock which nearly killed him It was called a heart attack but at no time did he have any symptoms or signs of heart disease Apparently he suffered from thrombosis of a fairly large intracranial artery because his character changed formerly a lovable good natured Irishman, he now became irascible formerly very clean and neat in every way now he had to be urged to bathe and change his linen formerly well mannered at table he now ate coarsely His employers saw the change and wondered if he were tippling in secret Later a little thrombosis hit his bulb and left his swallowing mechanism so impaired that with each meal food entered the larynx and caused a coughing spell This difficulty continued to the end of his life

Repeated medical examinations failed to show anything wrong except some hypertension

Then on a long journey he apparently had another stroke because again his character changed for the worse He became careless about many things he became more irritable and because of dribbling of urine his clothes began to reek of ammonia Highly significant of the great change in his mentality was the fact that he never seemed to notice the odor or to feel any embarrassment about it

Then one morning on getting out of bed he found one leg too weak to hold him up and at last his physicians began to suspect what was wrong with him Shortly after this his employers had to let him go He lived on for several years until the age of 57 Every few months there would come a dizzy spell or an attack of weakness and with each one of these shocks he died a little More and more his judgment failed Curiously however if he met an old friend or a stranger he could still for a few minutes pull himself together and be his old brilliant and merry self Soon however he would slump and become morose again His poor wife was nearly frantic trying to take care of him Finally one day there came the last stroke with a coma from which he never wakened he died a purely brain death with the heart and kidneys working well until the end

Case 4 — A woman at 56 was a stout tireless able person who had never been ill For long she had had a systolic blood pressure of 200 mm Hg but it had never bothered her Then after much overwork she began to fail and occasionally to have a dizzy spell with headache During the next 3 years these attacks pulled her down until she had to give up her work Then at 59 she had a big stroke with hemiplegia and complete aphasia but only slight mental confusion During the next few months her weight dropped from 190 to 100 pound (from 86 2 to 45 4 kg) Destructive changes promptly appeared in the right hip joint on the side of the paralysis Her blood pressure also dropped to normal The hemiplegia and aphasia soon cleared up but she was left for the rest of her days with great mental distress which was so awful that she craved death as a mode of escape

During the following 6 years she continued to have attacks of dizziness nausea and vomiting sometimes associated with mental distress Usually she was prostrated in bed for a few days afterward These were the attacks which are usually thought to be due to acute indigestion or Ménière s disease At 66 she died from a good sized cerebral

hemiplegia without loss of consciousness and without much if any clouding of the mental processes Because of this lack of any shock it is probable that often a little apoplexy may come during the day without the victim knowing it

Common Manifestations of the Disease

In innumerable cases in older persons it is impossible to tell at the time of the first consultations what is the meaning of a certain episode or the cause of a nervous breakdown which has come suddenly with feelings of exhaustion and weakness Only later as more episodes come or as a definite stroke appears or as the patient s mentality suffers or as his character and temperament change can one become fairly certain of what happened in the first spell

Sometimes a patient says that he slipped or stumbled or fell but the fact that for weeks or months afterward he was dizzy or unable to work or confined to a hospital will make it seem more probable that the fall was due to a slight stroke

Acute Indigestion — As already noted when an acute episode is associated with a storm going down the vagus nerves to produce nausea and vomiting and perhaps a curious paresthesia in the abdomen the first physician to arrive on the scene usually makes a diagnosis of acute indigestion Often if he would study the patient more carefully he would be told of a little numbness of an arm or a leg a tendency to fall to one side when walking or of difficulty in using the right hand or he would note some weakness of one side of the face or some difficulty in speaking or swallowing Often these phenomena clear up within a few hours or days and the patient then forgets to speak of them

Falling Down or Falling Out of a Chair — A common story is that the patient fainted or fell out of his chair Often he promptly picked himself up and then the essential part of the story is that afterward there came some paresthesia dizziness a little mental confusion or a change in character

For instance a production manager came because he had trouble in walking He had the typical shuffling gait of an old man The story obtained from his business associates was that some time before he had fallen out of his chair and from that moment on he was a changed man No longer would he initiate any thing and so far as possible he blocked initiative in his subordinates Then his legs became weak and finally he had to be retired because of his inefficiency That was years ago and he still shuffles and still is unable to do any work

Vertigo — One of the commonest symptoms that go with an episode is vertigo or more often a feeling of giddiness or uncertainty about standing or walking Rarely will there be deafness or ear noises to go with this Obviously not every attack of dizziness or uncertainty is due to a minor apoplexy but one should suspect this origin of the trouble particularly when the person is past middle age

in the morning while she was getting breakfast She fainted and sank to the floor For 6 hours after regaining consciousness she was mentally confused and kept asking over and over again what had happened With the fainting spell a strange feeling of distress and tingling shot into the left side of the thorax and abdomen As soon as she tried to eat, she found she could not take anything without getting the spasm in her abdomen A month later she had another little shock after which she had an aversion to food

On asking the husband if the e spells had brought any change in character he said Yes before this happened she was such a wonderful woman while now she is childish and forgetful and without interests and I have to watch over her all the time Four years later she had improved somewhat but still was depressed and far from normal

All these cases show that unless the physician happens to think of little apoplexies and asks about them he will never get the typical story, and he will never suspect what is the patient s real trouble

There are many more cases in which an older person complains of indigestion with much misery and feelings of weakness and fatigue and depression Especially when all the laboratory and roentgenologic studies are negative, the physician may suspect that the cause of the breakdown was a small apoplexy, but he will be unable to get any story of one The diagnosis will then have to remain indefinite until with the passage of time definite strokes appear

Symptoms

One of the most important points to recognize at the start is that a person can have a cerebral thrombosis bad enough to leave him with a damaged brain and inability ever to work again without causing any shock or great mental commotion Many a highly intelligent person has reported that during an attack he was fairly certain that he was having a stroke and yet felt no mental distress or confusion This absence of mental distress can explain why in innumerable cases, when it is obvious that an older person has suffered serious arteriosclerotic injury to the brain, it will be impossible to get any history of a small apoplexy The episode may have gone unnoticed or unrecognized early in the day or more probably it came during the night when the blood pressure was at its lowest and the tendency to thrombosis at its greatest

In many cases a severe morning headache may indicate that something went wrong during the night That a fairly large stroke need not wake the patient was shown by a college dean who woke one morning to find that most of his previously phenomenal memory was gone Aside from this he was perfectly well A few months later while at dinner he suddenly felt his cheek go numb and he was left with a permanent patch of anesthetic skin With this there was no mental confusion or even distress Other patients have been thrown to the ground and perhaps so weakened that they had to spend the night on the floor, but they felt no mental shock Others have suffered complete aphasia and

Distress Pain or a Paresthesia Referred out from the Brain into the Thorax or Abdomen — Many a small stroke produces as its first or main symptom a paresthesia pain distress flash of heat or rending feeling referred out into the thorax or abdomen When it occurs in the thorax the diagnosis generally is that of coronary disease When it occurs in the abdomen gastroenterologists usually spend months or years hunting for a lesion Similar disturbances are seen in some cases of encephalitis or brain tumor

Abdominal Distress Due to Increased Spasticity or Irritability of the Muscles or Nerves of the Wall in the Digestive Tube — Occasionally after a small stroke the stomach and small bowel will become so irritable reflexly active or spastic that the moment food or even water is swallowed there comes a painful spasm Usually after some months much of this spasticity or irritability fades, and the patient is able to eat again

Bulbar Paralysis — With a small apoplexy some patients get a slight bulbar injury which causes food to enter the larynx and to produce much coughing at table Other persons have ropy saliva such as is seen with some lesions of the brain Other patients begin to speak thickly

A Burning or a Bad Taste in the Mouth — Women past middle age sometimes complain of a bitter or metallic taste or a burning feeling in the mouth or tongue or palate In such cases nothing wrong can be seen in the mouth and the fact that in some cases the distress is felt in only half of the tongue or palate shows that it is due to an injury to some nerve or nerve center The fact that these distresses never are helped by any treatment and that they never go away suggests again that they are due to some irreparable injury to the nervous system

Slight Anesthesia or Numbness of the Skin or Weakness of Muscles or Ataxia — Many persons after a slight apoplexy complain of numbness or a slight temporary weakness of a hand or arm and others lose their ability to write easily or legibly

Changes in the Core of the Personality — As already noted with the first little stroke a person may become greatly changed and perhaps utterly miserable and without interest or joy in life Other persons who seem to have been hit much harder by the stroke so that they are left with some aphasia or hemiplegia will retain the core of their personality untouched and will go on as Pasteur did working hard and doing good work Thus a physician of 84 kept to the end of his life his interests his good humor his zest in life his good medical judgment and his good grooming in spite of the fact that in the last 5 years his memory for recent events was so destroyed that he could not even count off a dozen bills to pay a tradesman After counting 4 or 5 he would forget and have to start over again He kept on practicing medicine only by having constantly at his elbow his old office nurse who served as his memory for what he had done or started to do a few minutes before

Psychopathic Changes — Many persons after a small stroke become more or

and when following the attack there came some prostration or change in character or inability to work For instance a previously healthy man of 55 years one night had an attack of vertigo so bad that he could not walk without help The next day he went to work but for 10 days he was uncertain of his balance He suspected a stroke because his memory had suffered a bit and his writing was affected he often put down a word which was not the one that he intended to write He also for the first time in his life had severe morning headaches His blood pressure was normal

Nervous Breakdown — One of the commonest results of a small stroke is a nervous breakdown Whenever a person past middle life has a poorly explained nervous breakdown and especially one that came suddenly at a certain minute of a certain day or was there at dawning on a certain morning the physician always should think of the possibility that a small blood vessel in the brain has become thrombosed He must think of this all the more when with rest and good hygienic care months or years pass without any sign of improvement or recovery

Overemotionalism — Occasionally one of the most trying symptoms of an arteriosclerotic nervous breakdown will be a tendency to cry Often such crying is involuntary and not due to any feeling of sadness

Loss of Grooming — In many cases one of the surest signs to make one suspect that a man has had a small stroke is a loss of grooming or of a desire to keep the body clean and neat and well dressed It is highly significant of disease in the brain when an executive or a professional man begins to go around with his clothes spotted and unpressed and with his shoes unshined This may be the most important and perhaps the only neurological sign that can be found

The Significance of a Sudden Fall in Blood Pressure — When with an episode suggestive of apoplexy the previously high blood pressure drops to normal one must always suspect strongly that there was a small stroke If the physician is seeing the patient for the first time after an episode he may suspect that there used to be hypertension when he notes some cardiac enlargement or a ringing second aortic sound or a high diastolic pressure and decided hypertensive changes in the retinas In some cases then if the consultant will ask about it the patient will remember that someone told him he had hypertension or that his physicians remarked that the pressure dropped at the time of the spell Sometimes the pressure will remain normal for years afterward and sometimes it will climb back up again

Sudden Unexplainable Loss of Weight — Commonly after a small stroke there will be a sudden and decided loss of weight This may range from 15 to 100 pounds (6 8 to 45 4 kg) One suspects that it is due to an injury to one of the centers for homeostasis in the hypothalamus Occasionally the only sign of a small stroke will be this loss of weight Usually the weight then remains at the new level for the rest of the person s life

Distress Pain or a Paresthesia Referred out from the Brain into the Thorax or Abdomen — Many a small stroke produces as its first or main symptom a paresthesia pain distress ' flash of heat or rending feeling referred out into the thorax or abdomen When it occurs in the thorax the diagnosis generally is that of coronary disease When it occurs in the abdomen gastroenterologists usually spend months or years hunting for a lesion Similar disturbances are seen in some cases of encephalitis or brain tumor

Abdominal Distress Due to Increased Spasticity or Irritability of the Muscles or Nerves of the Wall in the Digestive Tube — Occasionally after a small stroke the stomach and small bowel will become so irritable reflexly active or spastic that the moment food or even water is swallowed there comes a painful spasm Usually after some months much of this spasticity or irritability fades and the patient is able to eat again

Bulbar Paralysis — With a small apoplexy some patients get a slight bulbar injury which causes food to enter the larynx and to produce much coughing at table Other persons have ropy saliva such as is seen with some lesions of the brain Other patients begin to speak thickly

A Burning or a Bad Taste in the Mouth — Women past middle age sometimes complain of a bitter or metallic taste or a burning feeling in the mouth or tongue or palate In such cases nothing wrong can be seen in the mouth and the fact that in some cases the distress is felt in only half of the tongue or palate shows that it is due to an injury to some nerve or nerve center The fact that these distresses never are helped by any treatment and that they never go away suggests again that they are due to some irreparable injury to the nervous system

Slight Anesthesia or Numbness of the Skin or Weakness of Muscles or Ataxia — Many persons after a slight apoplexy complain of numbness or a slight temporary weakness of a hand or arm and others lose their ability to write easily or legibly

Changes in the Core of the Personality — As already noted with the first little stroke a person may become greatly changed and perhaps utterly miserable and without interest or joy in life Other persons who seem to have been hit much harder by the stroke so that they are left with some aphasia or hemiplegia will retain the core of their personality untouched and will go on as Pasteur did working hard and doing good work Thu a physician of 84 kept to the end of his life his interests his good humor his zest in life his good medical judgment and his good grooming in spite of the fact that in the last 5 years his memory for recent events was so destroyed that he could not even count off a dozen bills to pay a tradesman After counting 4 or 5 he would forget and have to start over again He kept on practicing medicine only by having constantly at his elbow his old office nurse who served as his memory for what he had done or started to do a few minutes before

Psychopathic Changes — Many persons after a small stroke become more or

less psychopathic The physician must ask about such changes because usually they will not be mentioned to him by either the patient or the family For instance an elderly woman was brought to a physician for treatment of a carcinoma of the stomach diagnosed in her home town When this diagnosis could not be confirmed and the consultant noticed signs of an arteriosclerotic injury to the brain he asked the son if of late his mother had changed psychically "Yes,' he said that s curious since her fainting spell 6 months ago, she hasn't trusted me Formerly she adored me, but now she is so suspicious and secretive that the other day she wouldn t trust me even to deposit a little money in the bank for her She insisted on going herself Such changes in character are common and especially when they come suddenly they are very helpful in making the diagnosis

Moral Deterioration — Some old men with only one recognizable mild apoplexy will lose moral sense and will soon get into scrapes with prostitutes, girls or designing women Many lose their business judgment and begin to dissipate the family fortune Many a family has been ruined by the behavior of a man in this condition

Many Patients Become a Problem in the Home — The patient who has had one or more little strokes and a great change in character is often a terrible problem in the home He or she may make a prisoner of a spouse or a daughter and will cramp the lives of the grandchildren

A Tendency to Insanity May Be Brought Out — Occasionally what appears to be a small stroke will throw a patient into a disturbed mental condition which will resemble that of other members of the family who have gone insane

Agitated Depression — Not infrequently a small stroke or perhaps a fairly large one which is unrecognized at the time will throw the patient into an agitated depression or into a nervous state bordering on this Unfortunately the nature of this condition is commonly misunderstood by physicians who have never been taught to recognize it They are so concerned over the patient's complaints of constipation or discomfort in the abdomen that they fail to realize the importance of the fact that the woman is wringing her hands and weeping and saying that her mental suffering is more than she can bear or they fail to learn that unable to sleep she walks the floor every night in agony keeping the family all upset

Parkinson s Syndrome — A number of patients after small strokes wind up with a Parkinson s syndrome

Sudden Coming of Insomnia — When a person past middle age, who has always slept well suddenly and for no obvious cause finds himself or herself unable to sleep one must suspect that there must have been a small injury to some center in the hypothalamus which has to do with sleeping The trouble is similar to that which sometimes comes with an attack of encephalitis

Facial Pain — A number of the atypical, puzzling and intractable types of

pain in the face in older persons apparently are due to the little strokes As one would expect in these cases the injection of the nerves and tissues with large amounts of a solution of procaine will only numb the face and will not relieve the pain Evidently the cause for this is higher up in the brain

Sudden Blindness — Occasionally as when the thrombosis occurs in the artery of the optic nerve or in a large retinal vein the patient will suddenly go blind in one eye

Arthritis Coming Suddenly in Older Persons — Because in some persons with hemiplegia arthritis promptly appears in one or more joints of the weakened limb one must think of a minor apoplexy when in an older person some joint or a number of joints (as in the wrist) suddenly become badly inflamed and swollen and with trophic changes in the skin around them

A Flare up of an Old Migraine — A little apoplexy sometimes causes an old fairly silent migraine to flare up and cause much distress

Episodes without Permanent Residue Due Apparently to Spasm in a Small Blood Vessel of the Brain — A number of physicians in the past have described the type of attack which appears to be due to spasm in a small intracranial blood vessel In such cases a man may have aphasia lasting perhaps a half hour he will get perfectly well and in a few days or weeks he will have several repetitions of the trouble This certainly suggests that an artery has closed down and then opened again Occasionally a man will have an episode so severe that it leaves him with aphasia and a decided hemiplegia and yet he will be all straightened out within a few hours Many such cases reported in the literature show that also with this type of disease the patients go on and die with cerebral arteriosclerosis just as if they had been having little episodes of thrombosis

DIAGNOSIS

Because there are no laboratory tests or roentgenological examinations that will indicate to a physician that he is dealing with little strokes the diagnosis must be made from the history Even a complete neurological study will seldom turn up any defects in reflexes sensations or muscle strength The unfortunate feature is that rarely does a patient think of telling of a nervous breakdown with the all important changes in mentality and character Even the family rarely think to tell of the terrible problem they have at home and in the business For this reason the physician is almost certain to miss the correct diagnosis if he is not on the watch always for this disease and unless in many cases he gets a hunch that the person sitting there before him is not the person that he or she was a year or two before

In many cases this hunch can be gained by noting what a man s business is

less psychopathic The physician must ask about such changes because usually they will not be mentioned to him by either the patient or the family For instance an elderly woman was brought to a physician for treatment of a carcinoma of the stomach diagnosed in her home town When this diagnosis could not be confirmed and the consultant noticed signs of an arteriosclerotic injury to the brain he asked the son if of late his mother had changed psychically "Yes,' he said, that s curious since her fainting spell 6 months ago, she hasn't trusted me Formerly she adored me but now she is so suspicious and secretive that the other day she wouldn t trust me even to deposit a little money in the bank for her She insisted on going herself Such changes in character are common and especially when they come suddenly they are very helpful in making the diagnosis

Moral Deterioration —Some old men with only one recognizable mild apoplexy will lose moral sense and will soon get into scrapes with prostitutes, girls or designing women Many lose their business judgment and begin to dissipate the family fortune Many a family has been ruined by the behavior of a man in this condition

Many Patients Become a Problem in the Home —The patient who has had one or more little strokes and a great change in character is often a terrible problem in the home He or she may make a prisoner of a spouse or a daughter and will cramp the lives of the grandchildren

A Tendency to Insanity May Be Brought Out —Occasionally what appears to be a small stroke will throw a patient into a disturbed mental condition which will resemble that of other members of the family who have gone insane

Agitated Depression —Not infrequently a small stroke or perhaps a fairly large one which is unrecognized at the time will throw the patient into an agitated depression or into a nervous state bordering on this Unfortunately the nature of this condition is commonly misunderstood by physicians who have never been taught to recognize it They are so concerned over the patient s complaints of constipation or discomfort in the abdomen that they fail to realize the importance of the fact that the woman is wringing her hands and weeping and saying that her mental suffering is more than she can bear, or they fail to learn that unable to sleep, she walks the floor every night in agony keeping the family all upset

Parkinson's Syndrome —A number of patients after small strokes wind up with a Parkinson s syndrome

Sudden Coming of Insomnia —When a person past middle age who has always slept well suddenly and for no obvious cause finds himself or herself unable to sleep, one must suspect that there must have been a small injury to some center in the hypothalamus which has to do with sleeping The trouble is similar to that which sometimes comes with an attack of encephalitis

Facial Pain —A number of the atypical, puzzling and intractable types of

that it was one of a series one or more of which were typical little strokes At times in certain cases with our present knowledge it is impossible to say that a puzzling syndrome of great fatigue feelings of weakness and indigestion in an older p rson is due to cerebral arteriosclerosis but when during the next year or two the patient has a typical stroke or a series of them the attending physician will start wondering whether the first illness was also due to a stroke that came in the night

Apparently pathognomonic is a big fall in blood pressure or a sudden loss of weight following an episode Other important signs are failure of memory coughing and choking at meal times difficulty in writing or in pronouncing words burnings or distress in the mouth paresthesia throughout the body the sudden coming of insomnia overemotionalism an agitated depression or the sudden loss of vision in an eye

In some cases the physician must think of a brain tumor but usually with the passage of time and the lack of steady progression or signs of increased intra cranial pressure or destruction of certain nerves this possibility can be ruled out One has to think sometimes of the residue of an attack of encephalitis and in occasional cases the differential diagnosis between this disease and small apoplexies is impossible

Occasionally a roentgenogram of the base of the skull will show calcified internal carotid arteries and this will support the diagnosis of cerebral arteriosclerosis

Prognosis

The prognosis in these cases usually is poor and often hopeless When damage has been done to an important part of the brain and the patient has become apathetic and without any interest or joy in life there is not likely to be much recovery Aphasia with hemiplegia can disappear within a few days or weeks to leave the patient still energetic and efficient and happy and then again an unrecognized apoplexy coming during the night can leave the victim a hopeless wreck In the latter type of case there is little that can be done even in a palliative way

It is important that the physician make the correct diagnosis so that he will not injure his reputation by promising a cure It will help also to keep him from wasting his time on repeated overhaulings of the patient long treatments and perhaps from performing a futile operation or two In these cases it is bad to remove remaining teeth because commonly the patient cannot afterward wear plates his misery is greatly increased and he goes down hill more rapidly than before

In many cases the patient s family should be informed as to the situation so that they can prepare for the future Sometimes they must promptly sell a

Perhaps the record states that he is president of a good sized corporation and yet it is perfectly obvious that the seedy looking and mentally slowed up man on the other side of the desk could never hold such a position. Then the physician must ask and find that the man is not working and perhaps has not been for one or more years. Next questions must be asked to find out if the man's ill health came suddenly. Often the wife if questioned will tell of a day when her husband suddenly aged ten years or more and became almost a stranger to her. Business associates also can often date the man's illness from a certain day or week, when perhaps he "collapsed" or fell out of his chair.

In many cases a good consultant should make the diagnosis of premature senility the minute the patient walks in slowly, with uncertain and short steps. It may be noted also that the mental reactions to questioning are slow and the patient is unable quickly to understand or later to remember simple instructions in regard to the several examinations. Sometimes one will suspect that the man's face has lost expression or there will be a little twitching of the facial muscles on one side or a tendency to talk out of one side of the mouth or perhaps there will be a little drooling or there will be a little food left on the chin or on the clothes.

Occasionally there will be a tendency to whistle a bit when talking or to ho-hum often or to have peculiar tics. Sometimes there will be a tremor of the hands or of the head but this may be familial in type.

Too Much Emphasis May Be Paid to Unimportant Findings. — The physician can easily be deceived as to the diagnosis if during the examination he pays too much attention to little abnormalities that happen to turn up. If he is wise and experienced and thoughtful he will not be entirely satisfied with the diagnosis of an old coronary infarct or a heart murmur or an old duodenal ulcer or gall stones or diverticulosis of the colon. These red herrings drawn across the diagnostic trail must be disregarded because they cannot explain the great mental changes. The physician must remember that there is no abdominal disease which in a moment can change a bright wide awake, happy and efficient person into a dull, discouraged slowed up invalid who cannot work. This is the essential point.

One reason for the making of incorrect diagnoses in these cases is that a neurologist is practically never called. The family doctor who sees these patients first usually is so impressed by the fact that there are digestive distresses or pains in the thorax that when he calls a consultant he sends for either a gastroenterologist or a cardiologist but even when he calls in a neurologist the diagnosis will be missed if the neurologist does not understand that a big change in character, loss of memory or a soup stain on the coat is a neurological sign every bit as important as a positive Babinski or a Romberg sign.

Pathognomonic Symptoms. — Often the pathognomonic point is that the illness dates from a peculiar attack which came at a certain minute of a certain day. In other cases the most suspicious feature about a particular episode is

iodine because it has long been thought to keep arteries soft Lipoiodine is a pleasant preparation to take and one can give one or two tablets each day intermitting every two weeks for a few days to avoid getting cumulative effects

Soporifics may have to be given if the patient has much difficulty in sleeping Sedatives also may give a little relief from terrible mental anxiety and suffering Unfortunately no drug has yet been found to restore to these patients their old energy their sense of well being and their joy in living

In some cases physical therapy will be helpful especially when muscles are weak or when tissues and joints are aching In some cases sweat baths will be soothing and helpful

Many physicians will ask should the patient be told what is wrong with him? In many cases Yes So often the patient has a good idea as to what happened to him and he will have more faith in a physician who at least discusses the possibility that there was a little stroke The patient is happier also if he can frankly discuss the condition with someone It will take away some of his feeling of loneliness and fear

As always *one must tell the patient only that amount of truth which he* cares to face or which he can understand or react to properly Some persons prefer not to be told what is the matter with them and then obviously the truth should not be *forced on them* A few resent it and are outraged the more when other physicians seen later feel that the idea is preposterous Highly alarmist and neurotic or stupid persons therefore had better not be told In other cases *in which the physician feels that he had better say* something about an injury to the brain it will be less alarming to speak of a temporary spasm in a little blood vessel rather than of an irrevocable plugging by a thrombus Few persons *seem to object* to the idea of spasm and often it relieves their mind because it is less alarming than the thought of hemorrhage which had come to them This diagnosis has the great advantage also that it may be accepted by the physicians who later see the patient it is not so abhorrent to them as the idea of thrombosis

When the blood pressure is high or when there is severe morning headache it may help to give potassium thiocyanate in doses of from 3 to 9 grains (0 2 to 0 6 gm) a day The drug can be poisonous and therefore its administration should be watched and guided by determinations of the amount in the blood from time to time

If vertigo is troublesome the physician can try lowering the amount of sodium chloride in the diet or he can desensitize to histamine or try giving nicotinic acid or prostigmine

BIBLIOGRAPHY

1 CRITCHLEY M The neurology of old age (Goulstonian lecture) Lancet 1931 I 1119 1221 and 1331

business or they must guard the invalid so that he will not make bad investments and wreck the family fortune They must be advised not to waste all their savings on many overhaulings and foolish treatments Also, if they understand what has happened to the brain of their loved one they may be kinder, more sympathetic and more forgiving Business associates and employers should often know what is happening so that they can retire the man quickly before they suffer financial loss and perhaps the demoralization of a department

As already noted there are cases like that of Pasteur in which a severe stroke with hemiplegia does not keep the victim from doing good work for the remainder of a fairly long life

The Interval between Episodes — One encouraging fact is that some patients will have one or more definite small apoplexies and will then go for from 10 to 15 years without having another A man can even have so bad a stroke that he lies comatose for weeks finds himself afterward with a hemiplegia and aphasia and yet can recover beautifully

The big trouble with many persons who have had a small stroke, is that they go in daily dread of another one They must be exhorted not to do this and must be told that they may go 10 years or even more before another stroke comes

TREATMENT

The subject of treatment must be divided into that of the episodes and that of the disease

Treatment during an Episode — With a severe episode the patient will have to stay in bed for a few days at least until the dizziness and mental confusion pass Nowadays it is unfortunate that many of these patients are told that they have heart disease and are kept in bed for weeks or months and not allowed even to go to the bathroom Obviously if the patient hasn t coronary thrombosis he or she should be gotten up as quickly as possible Even when the physician makes the correct diagnosis he may keep the patient in bed too long because of fear that being up and about will bring another spell This fear is not justified by theory or experience The mistake is made of thinking that the stroke was due to hemorrhage Today it is known that hemorrhage is rare, and thrombosis is common As Naffziger some time ago pointed out since the little apoplexies are almost always due to thrombosis of a blood vessel it is not logical to try to lower the blood pressure actually it would be more logical to try to raise it

Often the family should be exhorted to ' let up on the aged relative and to stop hounding him or her to snap out of it' These persons cannot much help themselves when the brain is badly injured

Care of the Patient between Episodes — Since most patients and their families put their trust in medicine it is often well to give something and a good drug is

CHAPTER III

ENCEPHALITIS AND OTHER VIRUS INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

By GORONWY O BROUN

TABLE OF CONTENTS

2 CRITCHI FY M Discussion on the mental and physical symptoms of the presenile dementia Procced Roy Soc Med 1933 XXVI 1077
3 JANEW W J C A clinical study of hypertensive cardiovascular disease Arch Int M 1,11 XII 755
4 OSLER W Transient attacks of aphasia and paralysis in states of high blood pressure and arteriosclerosis Canad Med Assoc Jour 1911 I 919
5 ALVAREZ W C Small commonly unrecognized apoplexies Geriatrics 1946 I 189

September 1 1947

Among the virus infections of the nervous system there is one, rabies, which is so striking in its manifestations and so dramatic in its mode of spread that it was recognized readily even in ancient times. Rabies was known to Hippocrates and Aristotle as well as in all subsequent periods. The usual connection between the bite of a rabid animal and the onset of this disease, together with its painful spasmodic symptoms, readily distinguishes it ordinarily from all forms of encephalitis.

Poliomyelitis was the next virus infection of the nervous system to win definite clinical recognition. This disease was perhaps described by Underwood in England as early as 1774. Its separation as a distinct clinical entity dates from the work of Jacob von Heine[6] in Kolmar, Germany, in 1840. Strumpell[7] as long ago as 1885 showed that this disease occurs in an encephalitic form. Sometimes it occurs concurrently with epidemics of the summer types of encephalitis, thus complicating the differential diagnosis.

In 1890 Leichtenstern[8] observed cases of "influenzal" encephalitis during the pandemic of this disease which occurred at that time. About the same time a disease which was given the name of "nona" was described also. It has been suggested that this may have been a form of influenzal encephalitis, but in the disease entities recognized at the present time its place remains uncertain.

Since the viruses which cause influenza are now known, the relationship of these viruses to encephalitic infections occurring in association with this disease has been the subject of some study. It has not yet been established that the influenza viruses actually cause encephalitis in man[18,61].

If we study the medical texts[16] of the period of the early years of the present century, we find that recognition was given to the encephalitic form of poliomyelitis, to post-influenzal encephalitis as well as to that following other infectious diseases such as mumps and to toxic encephalitis, for example that occurring in lead poisoning. This represents the extent to which our knowledge of encephalitis had developed in the first decade of the present century.

During the course of the first World War numerous cases of an unusual type of infection involving the central nervous system were noted in Europe, probably first in Rumania[11] and somewhat later in France[1]. Finally, in 1917 a group of these cases were studied and described as a definite clinical entity by von Economo[5] of Vienna under the name of lethargic encephalitis. The onset of this illness occurred chiefly in the cooler months of the year.

7- ENCEPHALITIS AND OTHER VIRUS INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

Historical Account

The early history of encephalitis like that of other specific infections remains shrouded in uncertainty Somnolence and coma occurring during the course of febrile illness are phenomena so common and so striking that they could not well be overlooked even by the most unskilled observer The practice of careful clinical study, so strongly developed in the school of Cos naturally led to the recognition of cases of this type Hence it is not surprising that the writings of Hippocrates[1] record numerous instances of fever accompanied by delirium and coma In the Epidemics' several case reports appear in which findings still more suggestive of encephalitis are described Thus headache and neck rigidity coupled with fever delirium and coma are recorded in one instance and in another instance tremors of the hands and facial palsy accompanied by fever and delirium Following this period similar individual cases are reported often Occasionally even widespread epidemics are described which fit fairly well into the clinical picture of what we now call encephalitis Heckler[2] writing before the bacteriological era describes several epidemics of encephalitis" occurring in Germany in 1480 and 1481 and again in 1504, 1505 and 1517 In 1482 he notes an outbreak of febrile cerebritis in France and in 1529 a languor resembling syncope in Pomerania Sydenham[3] described an epidemic of febris comatosa observed in England in 1673-75 Stern[4] quotes a case described by Albrecht von Hildeshein in 1695 which appears to resemble closely the picture of lethargic encephalitis The occurrence of an outbreak of "sleeping sickness' in Tubingen in 1712 was noted by von Economo[5] in his first discussion of lethargic encephalitis

In all of these early descriptions of conditions suggesting encephalitis it is difficult to exclude in some instances the delirium and coma common to all overwhelming febrile illnesses and in others bacterial infections such as meningitis and brain abscess Until the development of the sciences of bacteriology and pathology and the introduction of the clinical study of the cerebrospinal fluid no reliable basis for these distinctions were available Therefore it is to be expected that our knowledge concerning the differentiation of virus infections of the nervous system from bacterial infections is largely of recent date The recognition of the multiplicity of types of encephalitis and the isolation and the study of the viruses giving rise to them are even more recent and no doubt still far from complete

Among the virus infections of the nervous system there is one, rabies, which is so striking in its manifestations and so dramatic in its mode of spread that it was recognized readily even in ancient times. Rabies was known to Hippocrates and Aristotle as well as in all subsequent periods. The usual connection between the bite of a rabid animal and the onset of this disease, together with its painful spasmodic symptoms, readily distinguishes it ordinarily from all forms of encephalitis.

Poliomyelitis was the next virus infection of the nervous system to win definite clinical recognition. This disease was, perhaps, described by Underwood in England as early as 1774. Its separation as a distinct clinical entity dates from the work of Jacob von Heine[6] in Kolmar, Germany, in 1840. Strumpell[7] as long ago as 1885 showed that this disease occurs in an encephalitic form. Sometimes it occurs concurrently with epidemics of the summer types of encephalitis, thus complicating the differential diagnosis.

In 1890 Leichtenstern[8] observed cases of "influenzal" encephalitis during the pandemic of this disease which occurred at that time. About the same time a disease which was given the name of "nona" was described also. It has been suggested that this may have been a form of influenzal encephalitis, but in the disease entities recognized at the present time its place remains uncertain.

Since the viruses which cause influenza are now known, the relationship of these viruses to encephalitic infections occurring in association with this disease has been the subject of some study. It has not yet been established that the influenza viruses actually cause encephalitis in man[181].

If we study the medical texts[10] of the period of the early years of the present century, we find that recognition was given to the encephalitic form of poliomyelitis, to post-influenzal encephalitis as well as to that following other infectious diseases such as mumps, and to toxic encephalitis, for example that occurring in lead poisoning. This represents the extent to which our knowledge of encephalitis had developed in the first decade of the present century.

During the course of the first World War numerous cases of an unusual type of infection involving the central nervous system were noted in Europe, probably first in Rumania[11] and somewhat later in France[12]. Finally, in 1917 a group of these cases were studied and described as a definite clinical entity by von Economo[5] of Vienna under the name of lethargic encephalitis. The onset of this illness occurred chiefly in the cooler months of the year.

Almost simultaneously with the recognition of lethargic encephalitis in Europe another disease was described in Australia, having many features in common with it This mysterious infection was called Australian X' disease[13 14] It occurs chiefly during the warmer months of the year in Australia and hence must be considered one of the "summer" types of encephalitis

In 1924 a definite and severe summer epidemic of encephalitis took place in Japan This was studied by many investigators including Kaneko and Aoki[15] and by them was distinguished from winter (lethargic) encephalitis by various clinical as well as seasonal features They suggested that the winter form of encephalitis be called type A the summer form type B Other epidemics of summer encephalitis occurred in Japan in 1929 1935 and 1937 and considerable numbers of sporadic cases were observed in the intervening years[16] Our knowledge of this infection recently has been increased through the studies of Sabin[14] and others associated with the American forces occupying Okinawa and the Japanese Islands

An epidemic infection very similar to Japanese encephalitis appeared in the United States during the summer of 1932 in Paris Illinois The following year it reappeared in and around St Louis Missouri[17] as well as in other parts of the mid western states This disease has been termed St Louis encephalitis It definitely has its highest incidence in August September and October

In 1933 and 1934 Rivers and Schwentker[18] described the accidental laboratory infection of human beings with 'louping ill , a virus disease of sheep which involves the central nervous system A form of encephalitis occurring chiefly in the spring and early summer has been recognized for a number of years in the U S S R [215] Casals [16] has found this disease to be serologically closely related to louping ill '

As early as 1925 Wallgren[19] gave a clinical description of cases of an unusual type of meningitis which he termed lymphocytic meningitis In 1934 Armstrong and Lillie [0] reported the isolation of a virus which subsequently they have shown to be the causative agent of this disease

Veterinarians have recognized an encephalomyelitis of horses for many years In 1931 the virus responsible for this disease in the western portion of the United States was described by Meyer Haring and Howitt[21] Several years later a different virus causing a similar infection in the eastern portion of the country was recognized by Ten Broeck

Human infection from both of these varieties of equine encephalomyelitis as well as a third variety now recognized in South America[140] is known to occur

In 1940 a neurotropic virus was isolated in Uganda Africa[40] which is known as West Nile encephalitis virus

The occasional isolation of viruses resembling that of herpes simplex from cases of lethargic encephalitis aroused interest in the possibility that this virus might be a cause of human encephalitis This fact was established through the isolation of the virus and the demonstration of intranuclear inclusion bodies in a fatal case of encephalitis by Smith Lenette and Reams[162]

The isolation of the virus causing mumps led to renewed interest in the neurological symptoms which follow this infection[16, 235]

While encephalitis following smallpox is rare[191] vaccination against this condition in certain European countries has been followed by encephalitis with sufficient frequency to cause considerable attention to be devoted to it[194] Chicken pox also occasionally is complicated by encephalitis[92]

Measles a known virus infection not infrequently is followed by the occurrence of encephalitis[185] The relation of the measles virus to this infection is not established but this must be recognized as a definite post infectious type of encephalities German measles likewise may have encephalitis as a sequel[188]

Pertussis considered to be of bacterial origin is complicated at times by evidences of damage to the central nervous system[14] Simple hemorrhages may be a possible cause but the occurrence of encephalitis can not be excluded

Infectious mononucleosis the cause of which still is obscure is followed by neurological symptoms with sufficient frequency to justify inclusion in this discussion[99]

CLASSIFICATION OF ENCEPHALITIS

The preceding review of the history of the recognition of the various forms of encephalitis indicates that a classification of the virus infections of the brain and meninges must take into consideration the specific types listed in the following outline

Almost simultaneously with the recognition of lethargic encephalitis in Europe another disease was described in Australia having many features in common with it This mysterious infection was called Australian X disease[14, 11] It occurs chiefly during the warmer months of the year in Australia and hence must be considered one of the "summer" types of encephalitis

In 1924 a definite and severe summer epidemic of encephalitis took place in Japan This was studied by many investigators including Kaneko and Aoki[1] and by them was distinguished from winter (lethargic) encephalitis by various clinical as well as seasonal features They suggested that the winter form of encephalitis be called type A the summer form, type B Other epidemics of summer encephalitis occurred in Japan in 1929 1935 and 1937 and considerable numbers of sporadic cases were observed in the intervening years[16] Our knowledge of this infection recently has been increased through the studies of Sabin[11] and others associated with the American forces occupying Okinawa and the Japanese Islands

An epidemic infection very similar to Japanese encephalitis appeared in the United States during the summer of 193- in Paris Illinois The following year it reappeared in and around St Louis Missouri[17] as well as in other parts of the mid western states This disease has been termed St Louis encephalitis It definitely has its highest incidence in August, September and October

In 1933 and 1934 Rivers and Schwentker[18] described the accidental laboratory infection of human beings with 'louping ill", a virus disease of sheep which involves the central nervous system A form of encephalitis occurring chiefly in the spring and early summer has been recognized for a number of years in the U S S R[215] Casals[16] has found this disease to be serologically closely related to louping ill

As early as 19-5 Wallgren[19] gave a clinical description of cases of an unusual type of meningitis which he termed lymphocytic meningitis In 1934 Armstrong and Lillie[20] reported the isolation of a virus which subsequently they have shown to be the causative agent of this disease

Veterinarians have recognized an encephalomyelitis of horses for many years In 1931 the virus responsible for this disease in the western portion of the United States was described by Meyer, Haring and Howitt[1] Several years later a different virus causing a similar infection in the eastern portion of the country was recognized by Ten Broeck

In addition to these certain bacterial, protozoal and toxic forms of encephalitis occur but will not be included in this discussion

The discovery of so many types of virus infections of the nervous system within a relatively short period of time has caused some confusion in regard to the classification of these diseases and has created problems in nomenclature epidemiology differential diagnosis prevention and treatment many of which remain unsolved

GROUP I

Types of encephalitis with time of onset chiefly, but not exclusively in the winter and early spring

(1) Encephalitis lethargica of von Economo, also called epidemic encephalitis and encephalitis type A of Kaneko and Aoki

(2) Herpes simplex encephalitis

(3) Post infectious encephalitis which includes

- (a) Post influenzal encephalitis
- (b) Encephalitis following measles and German measles
- (c) Encephalitis following small pox
- (d) Post-vaccinal encephalitis
- (e) Encephalitis following chicken pox
- (f) Encephalitis following mumps
- (g) Encephalitis accompanying infectious mononucleosis
- (h) Encephalitis following whooping cough

GROUP II

Types of encephalitis with time of onset chiefly in the late spring and early summer

(1) Russian spring summer tick-borne encephalitis, also called forest spring encephalitis Possibly identical with louping ill

GROUP III

Types of encephalitis with time of onset chiefly but not exclusively in the late summer and early autumn

(1) St Louis encephalitis
(2) Eastern equine encephalomyelitis
(3) Western equine encephalomyelitis
(4) Venezuelan equine encephalomyelitis
(5) Japanese type B encephalitis
(6) Australian 'X' disease
(7) West Nile encephalitis
(8) Encephalitic forms of poliomyelitis

GROUP IV

Encephalitis and virus meningitis with irregular seasonal distribution

(1) Lymphocytic choriomeningitis
(2) Louping ill
(3) Rabies

The work of von Economo was confirmed and extended by the Medical Research Committee of the British Ministry of Health[5] Marinesco and McIntosh working for this committee established definitely the fact that cases of encephalitis which were observed in England were identical with those described by von Economo in Austria and by Netter[6] in France and that encephalitis is a disease sui generis anatomically and clinically distinct from analogous affections

From 1917 onward cases of the disease were recognized in various parts of Europe[7] By the summer and autumn of 1918 the disease had been recognized in South America by Morquio[8] and in the United States by Neal[9] Subsequently the disease has been found in practically every country in the world An analysis of the figures on world incidence for the years 1919 to 1937 is given in Table I and shown graphically in Chart I The pandemic reached its peak in Europe in 19 0[3] but in Canada and the United States the year 19 3 marked the greatest incidence The available figures for the world incidence of the disease show very well defined peaks occurring in 19 0 and 19 4 with less evident peaks in 19 9 and 1933 From the time of the second peak in 19 4 to the present date there has been an almost continuous decline in the number of cases reported provided the summer cases of Japanese encephalitis and St Louis encephalitis are omitted

The first column in Table I shows the total number of cases of encephalitis reported throughout the world from 1919 through 1937 Cases of Japanese encephalitis and St Louis encephalitis are listed in separate columns The final column which shows the number of cases of encephalitis in each year after the known cases of summer encephalitis are subtracted is the best approximation that can be made of the world incidence of lethargic encephalitis

SEASONAL INCIDENCE

The ease with which lethargic encephalitis can be confused with a number of other virus infections of the brain renders the reports of its seasonal incidence subject to the errors of inaccurate diagnoses Nevertheless in the early years of the world wide pandemic which began in 1917 the higher incidence of encephalitis during the cooler months of the year was quite definite

The summary of official reports on seasonal occurrence of encepha

GROUP I

TYPES OF ENCEPHALITIS OCCURRING CHIEFLY IN THE WINTER AND EARLY SPRING

LETHARGIC ENCEPHALITIS

Synonyms — Encephalitis lethargica (von Economo), encephalitis type A (Kaneko and Aoki), winter encephalitis, epidemic encephalitis

Definition — Lethargic encephalitis is an infectious disease, probably caused by a neurotropic virus, occurring at all seasons but most commonly in the colder months of the year, characterized by focal lesions of the brain, involving particularly the basal ganglia, pons and medulla characterized by somnolence cranial nerve palsies and an irregular fever It exhibits a high initial mortality and in non fatal cases often is followed by serious chronic nervous sequelae

HISTORICAL ACCOUNT AND INCIDENCE

It is generally accepted that the first cases of lethargic encephalitis to be recognized occurred in Rumania during the months of April and May of 1915 [3] and were reported in 1916 under the title of "encephalite hemorrhagique avec un diplocoque encapsule" by Obregia Urechia and Carniol[11] In the following year 40 cases were reported from the French military hospitals by Cruchet Moutier and Calmettes[1] These cases had their dates of onset during 1915 and 1916 Further cases were reported by Etienne [4] some of which were seen during August of 1915 The cases of Etienne if accepted as being true cases of lethargic encephalitis indicate that the onset of some cases occurred during the summer time even at this early stage of the pandemic

Von Economo's report[5], which was given before the Vienna Society for Psychiatry and Neurology on April 17, 1917 usually is credited with being the first in which there was recognition of this disease as a definite clinical entity He also suggested the term lethargic encephalitis which has continued to be applied to this disease by many writers Von Economo s cases occurred in Vienna and had their onset in the early months of 1917

The work of von Economo was confirmed and extended by the Medical Research Committee of the British Ministry of Health. Marinesco and McIntosh, working for this committee, established definitely the fact that cases of encephalitis which were observed in England were identical with those described by von Economo in Austria and by Netter[6] in France, and that encephalitis is a disease sui generis, anatomically and clinically distinct from analogous affections.

From 1917 onward cases of the disease were recognized in various parts of Europe.[7] By the summer and autumn of 1918 the disease had been recognized in South America by Morquio[8] and in the United States by Neal[9]. Subsequently the disease has been found in practically every country in the world. An analysis of the figures on world incidence for the years 1919 to 1937 is given in Table I and shown graphically in Chart I. The pandemic reached its peak in Europe in 1920,[2] but in Canada and the United States the year 1923 marked the greatest incidence. The available figures for the world incidence of the disease show very well defined peaks occurring in 1920 and 1924, with less evident peaks in 1929 and 1933. From the time of the second peak in 1924 to the present date there has been an almost continuous decline in the number of cases reported, provided the summer cases of Japanese encephalitis and St. Louis encephalitis are omitted.

The first column in Table I shows the total number of cases of encephalitis reported throughout the world from 1919 through 1937. Cases of Japanese encephalitis and St. Louis encephalitis are listed in separate columns. The final column, which shows the number of cases of encephalitis in each year after the known cases of summer encephalitis are subtracted, is the best approximation that can be made of the world incidence of lethargic encephalitis.

Seasonal Incidence

The ease with which lethargic encephalitis can be confused with a number of other virus infections of the brain renders the reports of its seasonal incidence subject to the errors of inaccurate diagnoses. Nevertheless, in the early years of the world-wide pandemic, which began in 1917, the higher incidence of encephalitis during the cooler months of the year was quite definite.

The summary of official reports on seasonal occurrence of encepha-

litis given by the Matheson Commission for the years 1919-27 shows clearly the general seasonal trends[3] In the year 1920, which marked the first peak of this epidemic there was a marked increase of cases beginning in December of the preceding year and ending in May with the greatest incidence in February and March Subsequent years show this seasonal difference much less strikingly In 1924 a severe outbreak

TABLE I

WORLD INCIDENCE OF ENCEPHALITIS*

Year	*Total Cases From Available Official Reports*	*Total Japanese Type B Cases*	*Total Missouri Summer Cases*	*Total Cases Minus Known Summer Epidemic Cases*
1919	96			96
19 0	9 824			98 4
19 1	5 139			5 139
19 2	601			2,601
19 3	5 244			5 44
19 4	16 002	6 125		9 877
19 5	7 606	139		7,467
19 6	7 141	864		6 277
19 7	4 387	1 006		3 381
19 8	5 73	70		5 66
1929	7 763	2 058		5 705
1930	5 017	499		4 518
1931	4 385	129		4 256
1932	4 792	689		4 113
1933	7 6,4	791	1 648	5 235
1934	4,037	278	41	3 718
1935	8 542	5 370	19	3 153
1936	3 673	1 305	5	2 363
1937	4 65	2,030	518	1 717

These figures have been taken from the First Second and Third Reports of the Matheson Commission from the U S Public Health Service Weekly Reports from the U S Bureau of the Census Reports and also from the Reports of the Health Departments of St Louis City and St Louis County and Reports of the Missouri State Department of Health

of encephalitis took place in England Wales Scotland and Ireland This outbreak showed its greatest prevalence in June of that year and even the summer months of July and August showed a high incidence From this time onward the seasonal variation in cases of encephalitis in British Isles has been very slight

On the continent of Europe this 19 4 summer outbreak does not appear in the statistical reports and the predominance of winter cases while not so striking as in the early years of the pandemic still continues through the year 1929 However again referring to world incidence as shown in Table II on page 192 of the Matheson[11] report if all cases occurring in the winter and spring months that is from December of one year through May of the following year are totaled and compared with the total number of cases occurring in the summer and the autumn that is between June 1st and the end of November the first group predominates in each annual period The only exception to this rule would occur if the cases of the summer epidemic of encephalitis which occurred in Japan in 1924 are included

This reversal of seasonal distribution in the presence of an epidemic summer encephalitis is worthy of note and perhaps may be used in the detection of local increase even of sporadic cases of summer encephalitis in any locality At the time when summer epidemics occur the seasonal change in incidence stands out sharply The cases occurring between June and November definitely exceed those occurring between December and the end of May

The apparent decreasing seasonal specificity [3] of lethargic encephalitis may be due to an actual change in the seasonal character of the disease On the other hand in view of our increasing knowledge of the summer types of encephalitis it may be suggested that the general incidence of the winter cases has fallen to the point where sporadic cases of summer encephalitis now serve to level off the seasonal incidence This is even more likely to be the case in the United States and Japan where the summer types of encephalitis are known to be endemic

Age and Sex Incidence

Lethargic encephalitis occurs at all age periods but is most common in young adults Of 7 584 cases collected by the Matheson Commission [3] in which the age was stated the group between 20 and 30 years of age showed the highest incidence of occurrence Those between 10 and 20 years of age stand next In all other age groups there were fewer cases

Statistics indicate that approximately 60 per cent of the cases occur in males and 40 per cent in females [3] No special racial susceptibilities have been shown to occur[3]

Mortality

Mortality figures are extremely variable In a series of 3 558 cases, traced and investigated in England and Wales it was 33 5 per cent, varying considerably from year to year[3] During the extensive epidemic of 1924 the mortality rate was 27 9 per cent, while during the other years it has averaged 51 7 per cent In Switzerland during 1920 the case mortality rate was 29 5 per cent During the years 1921 to 1925 it was 64 [illegible] per cent In 7 876 cases collected from the literature by the Matheson Commission[3], the mortality was [illegible]0 5 per cent

During years of active epidemics there is more complete reporting of non fatal cases, and during such years the official figures ordinarily show a lower mortality percentage than in years of lesser incidence when fatal cases are reported but non-fatal cases often do not get into the official records It is noteworthy that in many countries, where encephalitis in recent years has been made a "reportable disease", the deaths reported as due to encephalitis often considerably exceed the number of "cases" reported

Little difference in mortality between the sexes is noted Occasionally a slightly higher mortality in males is observed Mortality is highest between fifty and sixty years of age but falls off in the higher age groups It is also high in the first years of life

Etiology

The etiology of lethargic encephalitis still remains uncertain A voluminous literature has accumulated on the subject, which has been reviewed carefully in the three reports of the Matheson Commission[16, 3, 30]

It is now conceded that this disease is entirely distinct from poliomyelitis The diseases differ in seasonal incidence, type of onset, usual symptomatology and distribution of pathological lesions Investigators have failed to recover the virus of poliomyelitis by inoculation of monkeys with encephalitis brain material and the convalescent serum of cases of lethargic encephalitis fails to show neutralizing antibodies[31] against the virus of poliomyelitis However the clinical differentiation in a given case between the cerebral bulbar and pontine forms of poliomyelitis and lethargic encephalitis may still occasionally constitute a problem in differential diagnosis

The possible relationship between influenza and encephalitis has long been the subject of argument Leichtenstern[8] described a type of encephalitis occurring in cases of influenza as long ago as the influenza epidemic of 1889 90 It would therefore appear that some form of encephalitis may occur not infrequently in association with epidemics of influenza Whether this encephalitis is identical with the lethargic encephalitis which occurred in pandemic form from 1917 to the present time is however a matter concerning which much controversy exists The more or less simultaneous occurrence of the pandemics of the two diseases in the period between 1917 and 19 1 the influenza like symptoms that not infrequently mark the onset of encephalitis and finally the appearance of evidences of parkinsonism and other nervous residuals known to follow encephalitis in individuals whose history showed a previous illness diagnosed only as influenza naturally raised this question However it would appear that cases of encephalitis were noted in Rumania and France prior to the onset of the influenza pandemic[31, 32] The possible identity of influenza and lethargic encephalitis was taken into consideration by von Economo[5] In his first classical description of the disease he notes that there was no unusual prevalence of influenza in Vienna at the time he observed his first cases of encephalitis

The pandemic of encephalitis obviously was of longer duration than the pandemic of influenza one of its years of greatest incidence being 1923 at which time the influenza epidemic definitely had ceased Strumpell[32] who observed both the encephalitis accompanying the previous epidemics of influenza and the epidemic of lethargic encephalitis considered the two conditions to be distinct disease entities This view was supported by Flexner[33] and is now generally accepted The possible relationship of the influenza viruses[34] to encephalitis will be discussed later It is admitted by many[3, 36, 37] however that an indirect relation may exist between influenza and encephalitis in that an attack of influenza may so lower resistance as to permit the invasion of the body by the causative agent of encephalitis

Toxic theories of the origin of encephaliti such as its relation to botulism[18] were investigated by the Medical Research Committee of the British Ministry of Health[25] They concluded that there was no relation between the two conditions

Much controversy has arisen regarding various bacteria which have been isolated by a number of workers from cases of lethargic encephalitis The earliest of these reports was that of von Weisner[39] who carried out the post-mortem studies on the first cases reported by von Economo

Mortality

Mortality figures are extremely variable. In a series of 3,558 cases, traced and investigated in England and Wales, it was 33.5 per cent, varying considerably from year to year[3]. During the extensive epidemic of 1924 the mortality rate was 27.9 per cent, while during the other years it has averaged 51.7 per cent. In Switzerland during 1920 the case mortality rate was 29.5 per cent. During the years 1921 to 1925 it was 64.2 per cent. In 7,876 cases collected from the literature by the Matheson Commission[3] the mortality was 50.5 per cent.

During years of active epidemics there is more complete reporting of non fatal cases, and during such years the official figures ordinarily show a lower mortality percentage than in years of lesser incidence, when fatal cases are reported but non-fatal cases often do not get into the official records. It is noteworthy that in many countries where encephalitis in recent years has been made a 'reportable disease", the 'deaths' reported as due to encephalitis often considerably exceed the number of 'cases' reported.

Little difference in mortality between the sexes is noted. Occasionally a slightly higher mortality in males is observed. Mortality is highest between fifty and sixty years of age but falls off in the higher age groups. It is also high in the first years of life.

Etiology

The etiology of lethargic encephalitis still remains uncertain. A voluminous literature has accumulated on the subject which has been reviewed carefully in the three reports of the Matheson Commission[16, 3, 30].

It is now conceded that this disease is entirely distinct from poliomyelitis. The diseases differ in seasonal incidence, type of onset, usual symptomatology and distribution of pathological lesions. Investigators have failed to recover the virus of poliomyelitis by inoculation of monkeys with encephalitis brain material and the convalescent serum of cases of lethargic encephalitis fails to show neutralizing antibodies[31] against the virus of poliomyelitis. However, the clinical differentiation in a given case between the cerebral, bulbar and pontine forms of poliomyelitis and lethargic encephalitis may still occasionally constitute a problem in differential diagnosis.

herpes was the source of the material used A monkey and two rabbits were inoculated intracerebrally The monkey and one rabbit remained symptom free The other rabbit became ill and died on the eighth day the brain showing lesions similar to those of encephalitis Later a second virus was obtained[52] from material from the nasopharynx of another case inoculated upon the scarified cornea of a rabbit A third virus was isolated and carried for a time[53] Together with these successful isolations there were many failures to secure viruses from encephalitic material

Introduction of material from encephalitic patients into rabbits by Kling and his coworkers[54] resulted in the reproduction of the picture of encephalitis The nature of the causative agent and its possible relation to herpes virus and spontaneous encephalitis in rabbits has been the subject of some controversy[55] A later article indicated that this agent was not filterable Koritschoner[56] and Kobayashi have isolated viruses from cases of encephalitis considered by some to be rabic virus[57, 59]

Doerr and Vochting[60] showed that encephalitis sometimes followed corneal implantation of herpes virus in rabbits Blanc[61] believed that certain resemblances could be shown between the herpes virus and the virus isolated by Levaditi Other viruses probably of the herpetic group were isolated by Doerr and Schnabel[62] Doerr and Schnabel[63] and Levaditi Harvier and Nicolau[64] have studied further the similarities and differences between herpes virus and that isolated from cases of encephalitis by Levaditi

The virus of Levaditi passes bacterial filters and is destroyed by antiseptics and bile It is killed also by heat of 55 C Rabbits may be infected by inoculation intracerebrally or into the sciatic nerve Also the scarified cornea or the anterior chamber of the eye scarified skin or inflamed nasal mucous membrane and the testicles have been successful routes of inoculation Very heavy doses given intraperitoneally or intramuscularly occasionally produced infection Intravenous subcutaneous and intracutaneous inoculations most often were unsuccessful In the sick animals the virus can be recovered from the brain and spinal cord not from the spinal fluid or blood The rabbit guinea pig monkey and mouse were susceptible to the virus White rats fowl and sheep were resistant

Virus neutralization tests with the serum of patient convalescent from encephalitis showed negative tests in five out of six cases The one patient who neutralized the virus had had the acute phase of the disease

The organism which he isolated, a diplo streptococcus, was accepted at first by von Economo as the causative agent, but later he considered it a saprophytic secondary invader[40]

Loewe Strauss and Hirshfeld[41], using Noguchi's ascitic fluid-kidney tissue media cultured spinal fluids, nasopharyngeal washings, naso pharyngeal mucous membrane and brain tissue from cases of encaphalitis and reported that they obtained growths of minute globular bodies occurring singly in pairs chains and clusters The reaction to Gram stain was variable The bodies would with some difficulty, pass bacterial filters Fifty per cent of rabbits inoculated with these cultures suc cumbed showing lesions considered typical of encephalitis at autopsy Flexner[38] was unable to cultivate this organism under similar circum stances and pointed out the frequency approximately 50 per cent, of 'spontaneous' encephalitis in the rabbit[4] This fact the occurrence of spontaneous encephalitis infections in the rabbit, has rendered question able much of the reported work on the causative agent of lethargic encephalitis Apparently at least three types of such infections have been noted[13 4 4] In addition the possibility of the spontaneous occur rence of herpes virus encephalitis in the rabbit still further complicates the picture

Rosenow in various experiments[46 47] has reported the isolation of streptococci with neurotropic tendencies from cases of lethargic enceph alitis In a later article[45] summarizing this work he concludes, 'the tenta tive conclusion seems warranted that this organism has etiologic signifi cance in each of the diseases studied' An evaluation of the possible etiological role of bacteria such as streptococcus viridans in encephalitis was made by McKinley[49] He considers the evidence for a bacterial origin of the disease to be highly doubtful Zinsser[50] has expressed similar opinions

The failure to recover bacteria regularly from the spinal fluid and tissues of cases of lethargic encephalitis and the resemblance of lethargic encephalitis, both in its clinical picture and its pathological lesions to other diseases known to be produced by filterable viruses has given to the virus theory of its causation popularity above all others

A number of viruses, identical with or somewhat resembling the virus of herpes have been found in cases of lethargic encephalitis by several workers The first of these was isolated by Levaditi and Harvier[51] in February, 1920 A patient, dying of encephalitis but also having facial

necrosis are rare and small Some increase in glial cells is noted Neuronophagia is at most slight in amount Ganglion cell degeneration occurs in cases of considerable duration These findings are typical of the acute stage of the disease

The findings in cases dying during the chronic stage of encephalitis are distinctly different A case is reported by Stern[4] autopsied six months after the onset of encephalitis Two months after onset this patient developed akinesia and marked hypertonic tremor with absence of spontaneous activity and marked weakness Four months later death occurred from an intercurrent infection At autopsy the brain showed practically no perivascular infiltrations or glial reaction The chief lesions were located in the region of the subthalamus lenticular nucleus and the substantia nigra and were in the nature of degenerative changes in ganglion cells with collections of pigment Lipoid degeneration likewise was noted in certain areas of the thalamus and hypothalamus

The other organs show few changes either in the acute or chronic stages of this disease A terminal pneumonia is seen occasionally Some fatty changes in the liver have been noted[67] and in some cases a slight cirrhosis Degenerative changes in the kidneys have been described also

Clinical Course

The original description of von Economo[5] covered most of the clinical features of the acute period of lethargic encephalitis The disease sometimes is of sudden sometimes of gradual onset The initial symptoms usually are headache and general malaise Certain mild symptoms of meningeal irritation are seen often but these ordinarily are not marked A slight stiffness of the neck a feeling of pressure in the eyeballs or a sensation of pounding in the head may be the chief manifestations Occasionally a definite Kernig's sign is noted After several days of symptoms such as these in the typical lethargic case somnolence develops The eyes remain closed and the patient sleeps continuously From this sleep however the individual can be aroused and may answer questions quite rationally Interspersed with the periods of sleep episodes of active delirium are likely to occur

The somnolence may deepen to stupor and coma and death occur after a week or after a more prolonged course Other cases may continue to sleep for weeks or even months and then gradually lose their

more than a year previously Cross immunity tests showed that the virus differed from that of poliomyelitis

Levaditi believes that man is rather resistant to encephalitis, requiring a lowered resistance to permit invasion of the nervous system by the virus He also believes the herpes virus must acquire enhanced neurotropic characters before it can cause encephalitis

As a possible explanation of the numerous failures to secure the virus from encephalitic brain material Levaditi suggests that the brain may contain neutralizing bodies against the virus He believes that the chances of isolating the virus are increased if the brain material is preserved for a while in glycerin Perdrau[6] lends support to this theory

The low percentage of virus isolations, the fact that herpes virus has been found in the spinal fluid of cases not having encephalitis and finally the low incidence of positive virus neutralization tests in the serum of convalescent encephalitis patients are the chief obstacles to the acceptance of the herpes like viruses as the etiological agent of lethargic encephalitis

The occurrence of intranuclear inclusion bodies in known cases of herpes encephalitis in animals and in man[162] and their absence in lethargic encephalitis casts doubt on the identity of these two disease conditions

From this brief review it will be seen that the question of the causative agent of lethargic encephalitis still awaits definite solution with the preponderance of evidence in favor of a virus perhaps related to that of herpes

Pathology

The gross findings in the brain of cases of lethargic encephalitis usually are not striking[5] The brain may appear entirely normal There may be a slight hyperemia a few small scattered hemorrhages slight edema rarely small areas of softening Both von Economo[5] and Stern[1] lay stress on the paucity of the hemorrhagic phenomena considering this as being in distinct contrast with post influenzal encephalitis Microscopically perivascular infiltrations chiefly of lymphocytes, but with occasional small groups of polymorphonuclear leucocytes are noted especially in the medulla pons the substantia nigra and other parts of the mid brain and the cerebral cortex Some degenerative changes occur in the vessel walls In cases of short duration areas of softening and

night, even marked insomnia are quite common both in the acute stages and as a residual of this disease Stern[4] states that as high as 20 per cent may show these symptoms

Headache is the most common disturbance of sensation It is present very frequently as an initial symptom and often persists during the acute stage Pains in the muscles of the extremities and neck are common Usually these disappear after the acute stage Rarely they may pass over into chronic neuralgic pains Headaches may persist also as a chronic symptom Vertigo may be present in the acute or chronic stages of the disease

Paralysis of the eye muscles is quite frequent Moritz noted pupillary disturbances in 75 per cent nystagmus in 60 per cent ptosis in 60 per cent double vision in 40 per cent Stern[4] in 200 cases from the literature found that 61 per cent showed eye muscle disturbance The same author found in 200 cases disturbances of cranial nerves other than those supplying the eye muscles in 50 instances 25 per cent Oculogyric crises a peculiar intermittent spasm of the ocular muscles lasting from a few minutes to half an hour or more are another common residual of lethargic encephalitis This results in a conjugate deviation of the eyeballs usually upward but occasionally to one side or downward

The disturbances of the skeletal muscle system include marked generalized lack of motor activity and loss of strength Stern[4] considers that this may be due in part to a poor transmission of motor nerve impulses as well as to the generalized weakness usually accompanying infections Certain irritative phenomena also are common as for example choreic movements and aimless tossing about also rhythmic clonic movements and rhythmic muscular tremors and muscular twitching occur These may be localized or general throughout the body Rarely epileptiform convulsions occur

Stern[4] has described several important types of disturbances in muscular tonus Three of the most important are akinetic hypertonia spastic athetosis and chorea like syndromes These conditions frequently pass over into the full picture of parkinsonism

Laboratory Findings

Occasionally albumin is found in the urine The leucocyte count varies between 5 000 and 20 000 with an average close to 10 000 The differential count may be normal or show a slight increase in stab forms

lethargy to recover or to pass over into some of the chronic sequelae of this disease

Fever occurs very irregularly in lethargic encephalitis Usually an elevation of temperature of moderate degree occurs at least for a few days sometime during the course of the illness, but some cases apparently are entirely afebrile No typical temperature curve can be described Neither does the temperature bear any relation to the somnolence or delirium of the patient

Certain paralytic symptoms commonly occur These are seen most often in the distribution of the cranial nerves but may be noted occasionally in the extremities The nerves supplying the eye muscles are affected most frequently Ptosis is common, beginning as a slight drooping of the lids, which the patient with some effort can overcome, and at times progressing to complete paralysis Oculomotor palsies very frequently occur with paralysis of various external ocular muscles Double vision is a very common symptom and may be the initial symptom of the illness Other cranial nerves may be involved also with facial asymmetry, deviation of the tongue, difficulty in swallowing and hiccough as clinical manifestations

Evidences of visceral lesions during the acute stages in general are rare Gastrointestinal symptoms are observed seldom Occasionally abdominal pain occurs Reys[67] believes that he has seen liver involvement with jaundice in the acute stage of encephalitis Cardiac murmurs are quite uncommon Some lowering of arterial tension is noted at times The lungs occasionally may be the site of secondary infection, and a pneumonia may be the terminal event in either acute or chronic stages of encephalitis Renal symptoms are rare

These clinical findings may be considered typical of the average case It must, however be pointed out that many cases present marked variations from this typical disease picture

Regarding the regularity of occurrence of some of the common symptoms the following illustrations may be given Lethargy, the symptom from which von Economo originally derived the name of this form of encephalitis is by no means universally found According to Stern[4] in 100 cases there occurred outspoken somnolence in 41 per cent transitory sleepiness in 9 per cent dream states in 3 per cent other drowsy or confused conditions in 14 per cent In general about 40 per cent show definite somnolence in all epidemics

Reversal of rest habits, sleeping during the day and restlessness at

night even marked insomnia are quite common both in the acute stages and as a residual of this disease Stern[1] states that as high as 20 per cent may show these symptoms

Headache is the most common disturbance of sensation It is present very frequently as an initial symptom and often persists during the acute stage Pains in the muscles of the extremities and neck are common Usually these disappear after the acute stage Rarely they may pass over into chronic neuralgic pains Headaches may persist also as a chronic symptom Vertigo may be present in the acute or chronic stages of the disease

Paralysis of the eye muscles is quite frequent Moritz noted pupillary disturbances in 75 per cent nystagmus in 60 per cent ptosis in 60 per cent double vision in 40 per cent Stern[1] in 200 cases from the literature found that 61 per cent showed eye muscle disturbance The same author found in 200 cases disturbances of cranial nerves other than those supplying the eye muscles in 50 instances 25 per cent Oculogyric crises a peculiar intermittent spasm of the ocular muscles lasting from a few minutes to half an hour or more are another common residual of lethargic encephalitis This results in a conjugate deviation of the eyeballs usually upward but occasionally to one side or downward

The disturbances of the skeletal muscle system include marked generalized lack of motor activity and loss of strength Stern[1] considers that this may be due in part to a poor transmission of motor nerve impulses as well as to the generalized weakness usually accompanying infections Certain irritative phenomena also are common as for example choreic movements and aimless tossing about also rhythmic clonic movements and rhythmic muscular tremors and muscular twitching occur These may be localized or general throughout the body Rarely epileptiform convulsions occur

Stern[1] has described several important types of disturbances in muscular tonus Three of the most important are akinetic hypertonia spastic athetosis and chorea like syndromes These conditions frequently pass over into the full picture of parkinsonism

Laboratory Findings

Occasionally albumin is found in the urine The leucocyte count varies between 5 000 and 20 000 with an average close to 10 000 The differential count may be normal or show a slight increase in stab forms

No constant changes in blood chemistry are noted other than those associated with dehydration. Slight increase in blood sugar accompanying increase in spinal fluid sugar has been noted occasionally. The blood Wassermann reaction is not affected by this disease.

The spinal fluid pressure in the acute stage is increased in many but not all cases. The fluid typically is water clear with little, if any, increase in protein content. Formation of a fibrin web and the occurrence of pigmentation of the fluid, while they have been reported, are rare[4]. Occurrence of hemorrhagic fluid probably is due in most instances to traumatism of vessels during the puncture since the nonhemorrhagic nature of the pathological process has been stressed.

The leucocyte count in the spinal fluid is quite variable. Many observers have found entirely normal counts, others elevated counts. Stern[4] states that he has collected from the literature 490 cases which showed an increased cell count during the acute stage, whereas 180 cases showed normal counts (see Table II). Usual counts are between 8 and 17 cells per cubic millimeter. Of 258 cited by Merritt and Fremont-Smith[68] 117 had cell counts below 10 per cubic millimeter. Marked increases to levels between 100 and 500 cells are rare. No definite connection between cell counts and type of symptoms has been established. In the chronic stages of the disease, even one to two months after the onset, the cell count usually is normal.

Regarding the types of leucocytes found in the spinal fluid, most observers find a preponderance of lymphocytes, although some observers, including von Economo, mention some cases in which the percentage of polymorphonuclear elements was increased.

The chloride content of the spinal fluid usually is normal. The glucose content of the spinal fluid sometimes is slightly increased, more often normal. Concentrations varying between 60 and 120 mgm. per 100 c.c. usually are found. This serves as an important differential finding in separating encephalitis from bacterial infections of the cerebrospinal system in which a definite decrease in sugar content is the usual occurrence. It does not differentiate this type of encephalitis from the other virus infections of the central nervous system, since in these also the sugar content is not decreased.

The colloidal gold reaction[83] usually is negative but in some cases may show a midzone change, rarely even a first zone curve. The Wassermann test in the spinal fluid, as in the blood, is negative except in cases complicated by syphilis.

Post Encephalitic Parkinsonism

The parkinsonian syndrome is one of the most common and distressing sequels of the winter type of encephalitis All authorities agree that the incidence of this condition is quite high Parsons[69] found that parkinsonism followed encephalitis in 25 per cent of 3 112 cases which he collected from England Scotland and Ireland Ashie Main[70] in a careful follow up study of a series of Glasgow cases found 19 1 per cent developed this sequel Reys from Strasbourg[87] reported 40 per cent Stern 58 4 per cent from Gottingen[4] Howe in a series of cases in

TABLE II — Spinal Fluid Cell Counts In Neurotropic Virus Diseases

Name of disease	*Number of Cases*	*Less than 7 cells per cu mm*	*7 250 cells per cu mm*	*251 1 000 cells per cu mm*	*1 001 to cells per cu mm*	*Types of leucocytes found*
Encephalitis lethargica	670	180 (27%)	490 (73%)	0	0	Nearly 100 lymphocytes
St Louis encephalitis	100	0	94 (94%)	5 (5%)	1 (1%)	Nearly 100 lymphocytes
Lymphocytic choriomeningitis	24	0	2 (8%)	10 (42%)	12 (50%)	75 to 100 lymphocytes
Eastern equine encephalomyelitis	8	0	2 (25%)	3 (37 5%)	3 (37 5%)	Granulocytes may predominate in early stages
Western equine encephalomyelitis	23	Few	Majority of cases average 130 cells	Very few	0	Adults above 80 lymphocytes children 50 granulocytes
Poliomyelitis	54	1 (2%)	47 (87%)	5 (9%)	1 (2%)	Nearly 100 lymphocytes

children in the vicinity of Baltimore found 20 per cent developed parkinsonism[2]

The syndrome consists of muscular rigidity tremors disturbances in gait and equilibrium and increased salivation The rigor is generalized but perhaps most marked in the face[87] Due to rigidity of the masseters there is difficulty in opening the mouth widely in mastication In later stages difficulty in swallowing may develop The face is mask like failing to show spontaneous movements and changes of expression with changes of emotions The voice may be jerky hurried thick and monot

onous Retention of a spirit of vivacity far out of proportion to the lack of vivacity as indicated by the voice and facial expression is seen often

The increase in salivation causes the patient to swallow continuously to care for the excess saliva Nevertheless in many cases it may drool from the mouth Next to the face the neck may show the most marked rigidity The two sides of the neck usually are involved equally holding the head more or less immovable but somewhat thrust forward and slightly flexed on the chest Occasionally the involvement is not equal on both sides and the head is rotated to one side or the other The deep muscles of the neck ordinarily are more involved than the sterno mastoid muscles

The trunk also takes part in the general muscular rigidity This makes turning movements in walking awkward exaggerated angular and with many interruptions and pauses Loss of normal associated movements contributes to this awkwardness The normal swinging of the arms in walking frequently is lost and the arms stay rigidly by the side The rigidity of the lower limbs makes walking difficult and to gether with the fixed position of the head and trunk so disturbs the center of gravity of the body as to lead to the type of locomotion characteristic of this condition There is a running staggering gait with the body somewhat bent forward The center of gravity being too far to the front the running gait appears necessary to prevent falling forward With this there may be difficulty in maintaining equilibrium

The upper extremities often are less involved than other regions but usually show some degree of rigidity With this there is also loss of ability to control the finer movements of the fingers frequently made worse by the occurrence of tremors

In addition to their occurrence in the upper extremities tremors may be noted in the face and lower extremities These are typically fine tremors during repose but become coarse when movement is attempted

Increased secretion of sebaceous glands is noted often giving the skin a peculiar greasy appearance This may be accompanied by ex cessive sweating Alteration in vasomotor functions with low blood pressure, cold hands and feet are seen not uncommonly Additional symptoms sometimes noted are difficulty in emptying the bladder and in moving the bowels Urinary incontinence is rare, but retention is not uncommon

Psychic Alterations

In addition to the serious nervous residuals, just described there are a number of psychic disturbances which are quite important During the acute stages it has been noted that apathy and somnolence are quite common and may deepen into true coma On the other hand excitement and violent delirium may occur

As a residual of this disease mental retardation and nervous instability and alterations of personality are the most common and most important Ashie Main[70] has given a number of illustrative case reports of these residuals

Mental retardation is of course largely limited to cases which had their onset in childhood and is evidenced by failure of normal mental development in the period following the acute phase of the disease There is dullness and failure to make normal progress in school In a series of 70 cases reviewed by Ashie Main[7] five years after onset mental retardation was noted in [illegible] In adults loss of memory and loss of power of mental concentration may be a counterpart of the mental dullness seen in children

Mental Instability

Mental instability is defined by Ashie Main as a condition of marked restlessness and excitability especially at night time This also is seen mostly in children Cases may show extreme emotionalism accompanied by whistling singing tossing and burrowing in bed tearing the bed clothes until utterly spent In these cases intelligence is good and there is no lack of moral ideas but mental instability is evident Some of these cases later pass over into still more serious conditions Ashie Main found five cases of this type in his series of 70 one year after the attack When reexamined five years after the acute attacks one of these cases had died one had developed perversion of conduct and three had developed parkinsonism

Nervous instability as a chronic residual manifests itself as insomnia drowsiness and irritability Such sequels are seen frequently in adults as well as children Ashie Main[7] found that 12 cases out of his series of 70 showed this type of disturbance five years after the acute attack Insomnia is somewhat more common than drowsiness

onous Retention of a spirit of vivacity far out of proportion to the lack of vivacity as indicated by the voice and facial expression is seen often

The increase in salivation causes the patient to swallow continuously to care for the excess saliva Nevertheless, in many cases it may drool from the mouth Next to the face the neck may show the most marked rigidity The two sides of the neck usually are involved equally holding the head more or less immovable but somewhat thrust forward and slightly flexed on the chest Occasionally the involvement is not equal on both sides and the head is rotated to one side or the other The deep muscles of the neck ordinarily are more involved than the sterno mastoid muscles

The trunk also takes part in the general muscular rigidity This makes turning movements in walking awkward exaggerated angular and with many interruptions and pauses Loss of normal associated movements contributes to this awkwardness The normal swinging of the arms in walking frequently is lost, and the arms stay rigidly by the side The rigidity of the lower limbs makes walking difficult and to gether with the fixed position of the head and trunk, so disturbs the center of gravity of the body as to lead to the type of locomotion characteristic of this condition There is a running staggering gait with the body somewhat bent forward The center of gravity being too far to the front the running gait appears necessary to prevent falling forward With this there may be difficulty in maintaining equilibrium

The upper extremities often are less involved than other regions but usually show some degree of rigidity With this there is also loss of ability to control the finer movements of the fingers, frequently made worse by the occurrence of tremors

In addition to their occurrence in the upper extremities tremors may be noted in the face and lower extremities These are typically fine tremors during repose but become coarse when movement is attempted

Increased secretion of sebaceous glands is noted often giving the skin a peculiar greasy appearance This may be accompanied by ex cessive sweating Alteration in vasomotor functions with low blood pressure, cold hands and feet are seen not uncommonly Additional symptoms sometimes noted, are difficulty in emptying the bladder and in moving the bowels Urinary incontinence is rare, but retention is not uncommon

Psychic Alterations

In addition to the serious nervous residuals, just described, there are a number of psychic disturbances which are quite important During the acute stages it has been noted that apathy and somnolence are quite common and may deepen into true coma On the other hand excitement and violent delirium may occur

As a residual of this disease mental retardation and nervous instability and alterations of personality are the most common and most important Ashie Main [9] has given a number of illustrative case reports of these residuals

Mental retardation is of course largely limited to cases which had their onset in childhood and is evidenced by failure of normal mental development in the period following the acute phase of the disease There is dullness and failure to make normal progress in school In a series of 70 cases reviewed by Ashie Main[78] five years after onset mental retardation was noted in In adults loss of memory and loss of power of mental concentration may be a counterpart of the mental dullness seen in children

Mental Instability

Mental instability is defined by Ashie Main as a condition of marked restlessness and excitability especially at night time This also is seen mostly in children Cases may show extreme emotionalism accompanied by whistling singing tossing and burrowing in bed tearing the bed clothes until utterly spent In these cases intelligence is good and there is no lack of moral ideas but mental instability is evident Some of these cases later pass over into still more serious conditions Ashie Main found five cases of this type in his series of 70 one year after the attack When reexamined five years after the acute attacks one of these cases had died one had developed perversion of conduct and three had developed parkinsonism

Nervous instability as a chronic residual manifests itself as insomnia drowsiness and irritability Such sequels are seen frequently in adults as well as children Ashie Main[79] found that 12 cases out of his series of 70 showed this type of disturbance five years after the acute attack Insomnia is somewhat more common than drowsiness

Alterations of personality and perversion of conduct is an extremely distressing residual of encephalitis This may occur with or without symptoms of parkinsonism The most common personality change is marked irritability The individual develops a violent temper and is irritated and excited by incidents which prior to the attack of encephalitis would not have disturbed him In some individuals, most of whom are children, the change amounts to complete perversion of conduct These children may be impulsive destructive and violent They may lie and steal and show exaggerated erotic and sexual tendencies While not feeble minded in a technical sense they may be mentally defective in respect to morals Definitely criminal behavior may follow The seriousness of the ultimate prognosis of lethargic encephalitis is well illustrated by referring again to the analysis of 70 cases by Ashie Main[0] Incomplete recovery marked by such conditions as mental retardation mental instability nervous instability and physical defects were noted in 20 cases A total of 18 cases developed definite parkinsonism and of these eight also showed evidence of abnormal mental reactions Twenty one cases died, 18 of these terminated fatally between six days and five months after the onset Three others died of parkinsonian complications between one and three years after the onset of encephalitis Five cases were eliminated as of doubtful diagnosis Seven cases only showed complete recovery after five years

Howe[11] has analyzed similarly a group of 66 children who suffered attacks of encephalitis in the vicinity of Baltimore Maryland In this group 4 per cent made complete recoveries after a five year period

Dimsdale[-0] in 1946 reviewed 3 0 cases of the parkinsonian syndrome and pointed out certain difference between those which followed a definite attack of encephalitis and those which had no history of encephalitis One hundred cases were reviewed which occurred between 1900 and 1919 prior to the epidemic of lethargic encephalitis Most of these developed symptoms between the ages of 51 and 60 years The principal symptom and objective sign was tremor, most marked on the right side of the body Abnormal mental states ocular symptoms and excessive salivation were rare One hundred additional cases were seen between the years 1920 and 1930 Thirty four of these resembled the previous group Fifty four of this group followed shortly after a recognized attack of lethargic encephalitis Shakiness was the most common symptom but muscular rigidity was marked on physical examination Mental symptoms and disorders of sleep, ocular symptoms and

excessive salivation were common Eleven cases had symptoms resembling the postencephalitic group but had no history of an attack of encephalitis One hundred and twenty cases were studied between 1931 and 1942 Fifty two appeared to conform to the type of case seen in the years prior to 1919 Twenty four had a history of an attack of encephalitis although a long latent period usually was noted between the attack of encephalitis and the onset of parkinsonism Forty two cases appeared to resemble the post encephalitic type but gave no definite history of encephalitis Muscular rigidity was a marked feature of this group and the age distribution was such that they would have been young adults at the time when the epidemic of lethargic encephalitis was at its height

Differential Diagnosis

The acute somnolent types of winter encephalitis can be confused with bacterial forms of meningitis as well as with lymphocytic choriomeningitis herpetic and post infectional encephalitis sporadic post seasonal cases of St Louis encephalitis equine encephalomyelitis and encephalitic forms of poliomyelitis The points of value in differentiation are

1 Seasonal incidence lethargic encephalitis is more common between December and May while other types of encephalitis are more common in late summer and autumn Lymphocytic choriomeningitis occurs at any season The post infectional types of encephalitis have a seasonal distribution quite similar to that of lethargic encephalitis

2 Age incidence winter encephalitis occurs at all ages but is most common in late childhood and early adult life This contrasts with the encephalitic forms of poliomyelitis which particularly attacks young children and St Louis encephalitis which shows increasing incidence with advancing years The post infectious types of encephalitis are more common in relatively young children Lymphocytic choriomeningitis has about the same age incidence as lethargic encephalitis

3 Epidemiological distribution lethargic encephalitis has a world wide distribution but rarely with any great concentration of cases in a limited area St Louis encephalitis like Japanese B encephalitis shows sharply localized epidemics Equine encephalomyelitis occurs like St

Alterations of personality and perversion of conduct is an extremely distressing residual of encephalitis This may occur with or without symptoms of parkinsonism The most common personality change is marked irritabilty The individual develops a violent temper and is irritated and excited by incidents which prior to the attack of encephalitis would not have disturbed him In some individuals most of whom are children the change amounts to complete perversion of conduct These children may be impulsive destructive and violent They may lie and steal and show exaggerated erotic and sexual tendencies While not feeble-minded in a technical sense they may be mentally defective in respect to morals Definitely criminal behavior may follow The seriousness of the ultimate prognosis of lethargic encephalitis is well illustrated by referring again to the analysis of 70 cases by Ashie Main[70] Incomplete recovery marked by such conditions as mental retardation mental instability, nervous instability and physical defects were noted in 20 cases A total of 18 cases developed definite parkinsonism and of these eight also showed evidence of abnormal mental reactions Twenty one cases died 18 of these terminated fatally between six days and five months after the onset Three others died of parkinsonian complications between one and three years after the onset of encephalitis Five cases were eliminated as of doubtful diagnosis Seven cases only showed complete recovery after five years

Howe[71] has analyzed similarly a group of 66 children who suffered attacks of encephalitis in the vicinity of Baltimore, Maryland In this group 42 per cent made complete recoveries after a five year period

Dimsdale [0] in 1946 reviewed 320 cases of the parkinsonian syndrome and pointed out certain difference between those which followed a definite attack of encephalitis and those which had no history of encephalitis One hundred cases were reviewed which occurred between 1900 and 1919 prior to the epidemic of lethargic encephalitis Most of these developed symptoms between the ages of 51 and 60 years The principal symptom and objective sign was tremor most marked on the right side of the body Abnormal mental states ocular symptoms and excessive salivation were rare One hundred additional cases were seen between the years 1920 and 1930 Thirty four of these resembled the previous group Fifty four of this group followed shortly after a recognized attack of lethargic encephalitis Shakiness was the most common symptom but muscular rigidity was marked on physical examination Mental symptoms and disorders of sleep, ocular symptoms and

excessive salivation were common Eleven cases had symptoms resembling the postencephalitic group but had no history of an attack of encephalitis One hundred and twenty cases were studied between 1931 and 1942 Fifty two appeared to conform to the type of case seen in the years prior to 1919 Twenty four had a history of an attack of encephalitis although a long latent period usually was noted between the attack of encephalitis and the onset of parkinsonism Forty two cases appeared to resemble the post encephalitic type but gave no definite history of encephalitis *Muscular rigidity was a marked feature of this* group and the age distribution was such that they would have been young adults at the time when the epidemic of lethargic encephalitis was at its height

Differential Diagnosis

The acute somnolent types of winter encephalitis can be confused with bacterial forms of meningitis as well as with lymphocytic choriomeningitis herpetic and post infectional encephalitis sporadic post seasonal cases of St Louis encephalitis equine encephalomyelitis and encephalitic forms of poliomyelitis The points of value in differentiation are

1 Seasonal incidence lethargic encephalitis is more common between December and May while other types of encephalitis are more common in late summer and autumn Lymphocytic choriomeningitis occurs at any season The post infectional types of encephalitis have a seasonal distribution quite similar to that of lethargic encephalitis

2 Age *incidence* winter encephalitis *occurs at all ages but is* most common in late childhood and early adult life This contrasts with the encephalitic forms of poliomyelitis which particularly attacks young children and St Louis encephalitis which shows increasing incidence with advancing years The post infectious types of encephalitis are more common in relatively young children Lymphocytic choriomeningitis has about the same age incidence as lethargic encephalitis

3 Epidemiological distribution lethargic encephalitis has a world wide distribution but rarely with any great concentration of cases in a limited area St Louis encephalitis like Japanese B encephalitis shows sharply localized epidemics Equine encephalomyelitis occurs like St

Louis encephalitis in fairly well localized areas often in association with that infection

4 Clinical course, in lethargic encephalitis there is an ill defined temperature change which rarely is greatly elevated and has no relation to the severity of symptoms The febrile reaction may be slight and of brief duration in cases in which the phase of somnolence and acute neurological symptoms may continue for many weeks or even months This contrasts with the usual definite febrile reaction of bacterial meningitis, the St Louis type of encephalitis, equine encephalomyelitis and lymphocytic meningitis As a rule these diseases terminate in death or recovery in one to three weeks In St Louis encephalitis the severity of symptoms definitely runs more or less parallel with the severity of the fever This is true also of the equine types of encephalomyelitis

Poliomyelitis has a brief initial fever and from then onwards usually is afebrile The early onset of paralyses of the extremities serves to distinguish poliomyelitis from the encephalitis group of infections in most cases

Ocular and other cranial nerve palsies are much more common in lethargic encephalitis than in any other variety of encephalitis although such palsies are present in a small percentage of cases of the St Louis type The persistence of cranial nerve palsies beyond the period of febrile reaction is much more typical of the lethargic type of encephalitis than of any other

The akinetic and hyperkinetic types of lethargic encephalitis particularly when they occur in afebrile cases and extend over a long period of time, are typical of lethargic encephalitis and very rare in any other type The same is true of the occurrence of the parkinsonian syndrome either in the acute or chronic stages The occurrence of serious, chronic, nervous residuals is far more common in lethargic encephalitis than in any other, except perhaps eastern equine encephalomyelitis where in the few surviving cases severe residuals have occurred

The laboratory findings in the various forms of encephalitis and meningitis differ chiefly in the blood and spinal fluid findings The peripheral blood in the purulent forms of bacterial meningitis shows usually a distinct polymorphonuclear leucocytosis This is absent often in tuberculous meningitis The various types of encephalitis including lethargic encephalitis, show at most a mild leucocytosis, and often little change in the cellular elements of peripheral blood is found

Purulent bacterial meningitis may show a positive blood culture The blood culture in encephalitis is negative

The spinal fluid findings are of even greater diagnostic importance In purulent bacterial types of meningitis the organism causing the infection usually is demonstrable either by direct smear or by cultural methods Even in tuberculous meningitis the tubercle bacillus may be demonstrated often All of the viruses causing encephalitis are ultramicroscopic in size and will not grow on ordinary culture media

The examination of the cells of the spinal fluid is also of considerable diagnostic value In lethargic encephalitis the spinal fluid often may show a normal cell count and usually shows less than 20 cells per cu mm Very high counts are rare The average counts are lower than those of St Louis encephalitis equine encephalomyelitis and distinctly lower than that of lymphocytic meningitis The other usual spinal fluid findings are a clear fluid with slight increase in pressure slight protein increase normal or somewhat high sugar content The differential count of the cells of the spinal fluid shows chiefly lymphocytes All of these findings occur in the other virus infections of the central nervous system They do serve to differentiate this infection from purulent forms of meningitis in which the cell count is quite high granulocytes predominate in the differential count and the spinal fluid sugar content and spinal fluid chlorides are reduced in quantity It should be mentioned also that some cases of eastern equine encephalomyelitis show a predominance of granulocytes in the spinal fluid Tuberculous meningitis may show a lymphocytic pleocytosis in the spinal fluid in the early stages but usually at least 20 per cent of the cells are granulocytes[68]

In the types of meningitis due to pyogenic bacteria the cell count in the spinal fluid usually is high ordinarily above 1 000 per cu mm and the differential count shows a marked preponderance of granulocytes The protein content of the spinal fluid is increased much more markedly in the bacterial types of meningitis than in the various forms of encephalitis due to virus infection The sugar content of the spinal fluid usually is normal or may be even slightly increased in encephalitis In both tuberculous meningitis and meningitis due to pyogenic bacteria the sugar content of the spinal fluid is definitely decreased except in the early stages of the disease A similar difference is found in the chloride content of the spinal fluid This remains near normal levels in the various forms of encephalitis whereas usually it is definitely decreased in bacterial infections of the brain and meninges

Since the identity of the causative virus of lethargic encephalitis still

is uncertain it is not possible at this time to establish the diagnosis by virus isolation Neither can we make use of virus neutralization tests or complement fixation tests to establish a positive diagnosis These tests however, can be used to exclude those types of virus infections which cause encephalitis and in which the causative virus is available These tests are of value in excluding St Louis encephalitis the equine encephalomyelitis lymphocytic meningitis and others

Treatment

Because of the uncertainty of the identity of the causative agent in lethargic encephalitis little can be said regarding preventive measures The rarity of any evidence of contagion has been noted by all students of the disease The concentration of cases in a given area has seldom been such that drastic measures of isolation seemed indicated The infrequency with which multiple cases occur in the same family suggests that spread may take place largely through healthy carriers

Specific Treatment

In attempts at specific treatment a number of antibacterial sera and vaccines have been employed Neal[171] in 1942 reported the results of the extensive and careful work of the Matheson Commission on the treatment of lethargic encephalitis Attention was given particularly to herpes virus believed by Levaditi[51] to be the causative agent of encephalitis, and to the green producing streptococcus which Rosenow[47, 48] and Evans and Freeman[110] believe to be the cause

Vaccines were prepared from the brain material of rabbits injected intracerebrally with herpes virus Levaditi s strain C of herpes virus was used in the earlier work but this virus soon lost its virulence Later a strain of herpes virus isolated by Perdrau was used to test the immunity of rabbits previously inoculated with sublethal doses of a different strain of herpes virus The vaccine prepared from the brains of the rabbits which were found to be immune to the second herpes virus inoculation was termed hyperimmune rabbit brain vaccine X' These rabbits were also bled and the hyperimmune serum was used in the treatment of a small number of patients with acute encephalitis The serum

treatments were soon discontinued on account of the occurrence of severe serum sickness A third vaccine was prepared by Gay and Holden in 1933 This consisted of a formalinized herpes virus

A control series of cases received injections of normal rabbit brain Alternate cases were treated for a time with Rosenow s streptococcus vaccine and injections of the rabbit brain vaccines The herpes virus vaccine was given intramuscularly at daily intervals for the first few weeks and then twice weekly until a total of 100 c c of vaccine had been given

The results with the herpes virus vaccines were much better than those secured with the Rosenow streptococcus vaccine The formal inized vaccine F appeared superior to the rabbit brain vaccine X

Cases treated with vaccine F and X showed a mortality in the acute stage of 11 8 per cent compared to 4 6 per cent in untreated cases In the chronic stage untreated cases showed improvement in only 7 6 per cent of the observed cases When treated with the Rosenow strepto coccus vaccine only 4 5 per cent were improved With rabbit brain vaccine X improvement was seen in 16 9 per cent of the chronic cases With the formalinized herpes virus vaccine F 54 6 per cent of the chronic cases treated from six months to five years showed improvement *This result with the formalinized herpes virus vaccine presents the most encouraging picture of any form of treatment so far suggested for lethargic encephalitis*

Chemotherapy

Efforts at chemotherapy have included use of dyes such as acri flavine trypaflavine and gentian violet and arsenicals such as sodium cacodylate arsphenamine neoarsphenamine and tryparsamide Various bismuth preparations and tartar emetic were tried No definitely benefi cial effects have been secured from any of these preparations Von Economo[73] has suggested the intravenous use of a 10 per cent solution of sodium iodide in doses up to 100 c c With this he also used urotropin (methenamine)

The more recently developed antibiotics such as the sulfa drugs penicillin and streptomycin have apparently no curative value in virus infections in general and no effect has been reported in lethargic en cephalitis They can be of distinct value however in preventing and treating secondary bacterial infections which may occur as complica

tions of encephalitis Good use can be made of these agents in treating complicating pneumonia and ascending infections of the urinary tract

General Measures

Skillful and conscientious nursing care is an essential feature of the treatment of encephalitis Particular attention must be given to measures which will insure adequate nutrition during the long periods of somnolence in the acute stage and to the patients disabled by parkinsonism in the chronic stage Administration of parenteral fluids and use of the nasal tube for feeding patients often are indicated The diet must be adequate in all essentials including the vitamins Attention must be given to the prevention of hypostatic pneumonia by frequent change of position as likewise to the prevention of decubitus The disturbances in the nervous control of the urinary bladder and rectal sphincters which are encountered sometimes call for careful observation of the urine for evidence of ascending infection

Where spinal fluid pressure is found to be high, repeated spinal puncture or use of hypertonic glucose or surcrose solutions intravenously may be of value

Treatment of Nervous Sequelae

After the acute phase of the illness has passed the frequent occurrence of the chronic nervous sequelae particularly parkinsonism, has called urgently for the development of effective therapeutic aids The experience of the last twenty years has led to the conclusion that derivatives of belledonna and stramonium are probably the most effective agents at our disposal Many physicians have used the pure alkaloids atropine and hyoscine There is no question that a measure of relief from the symptoms of parkinsonism usually can be secured by the use of either or both of these alkaloids

An example of the method of use of *atropine* is that of Kleemann[74] The alkaloid is administered in the form of 0 5 per cent solution beginning with one minim (0 065 c c) twice daily and increasing by 1 minim (0 065 c c) twice daily until there is no further subjective or objective improvement After continuing at this level for some time the dose is reduced gradually until the first increase in unfavorable symptoms is

noted When the most effective dose has been determined this is given in tablet form

Hyoscin also has been used widely Its most effective dose also must be determined for each individual case beginning with an initial dose of gr 1/200 (0 3 mgm) of the hydrobromide two or three times daily

Apparently one of the most effective of the treatments proposed for post encephalitic parkinsonism is the *Bulgarian treatment* This consisted in its original form of a white wine decoction of the root of the Bulgarian belladonna plant A Bulgarian apothecary Ivan Raeff was the first to make this preparation The treatment was popularized in Italy by Panegrossi[75] and has now been used in many other countries Neal[76] and Fabing[77] reported on its use in the United States It is claimed that the effect of the total alkaloids of the Bulgarian belladonna root is superior to that of the pure alkaloids such as atropine and hyoscine Most of those who have employed this treatment have been well impressed with its effectiveness Neal[76] believes that it probably offers the best available symptomatic treatment for postencephalitic nervous residuals

When used in the form of the decoction the usual initial daily dose is 2 to 3 c c (30 to 45 minims) given once daily This is increased by 1 to 3 c c (30 45 minims) daily until 20 c c (ʒ 5) are reached The daily dose then is divided and half given at 11 00 A M and half at 11 00 P M The total daily dose then is increased until the most effective dose is reached usually somewhere between 20 c c (ʒ 5) and 60 c c (℥ 2) Occasionally as much as 90 c c (℥ 3) has been given

The decoction of Bulgarian belladonna plant is said to contain an average of 0 2 mgm of total alkaloids per cubic centimeter The treatment has also been used in tablet form each tablet containing 0 4 mgm of total alkaloids Starting with a single tablet the dose is increased by one tablet daily until the best effect is secured Dryness of the mouth blurring of vision dizziness headaches vomiting diarrhea and difficulty in urination are symptoms of overdosage and call for halting the increase or decreasing the dose of the drug The treatment is not recommended in the presence of hepatic renal myocardial or prostatic disease Cases of idiopathic parkinsonism are said to tolerate this treatment poorly

Stramonium also has been used widely in the treatment of *post encephalitic parkinsonism*[78] *Treatment usually is administered in the* form of the tincture the extract or the dried leaves Tolerance to this drug must be determined by gradually increasing the dosage in each case

Benzedrine sulfate is another drug which has been used in the treat

ment of parkinsonism Favorable reports on its use have been published by Prinzmetal[9], Davis and Stewart[80] and Matthews[81] Doses of 5 to 10 mgm, once or twice daily, ordinarily have been employed, although doses as high as 30 mgm occasionally have been given

Fever therapy has not been found to be effective in encephalitic parkinsonism The same is true of various forms of shock therapy such as injections of foreign protein

Curare as d tubocurarine in aqueous solution will relax temporarily the muscular spasticity of cases in the parkinsonian syndrome, but its action is so brief as to be of little value The introduction of suspensions of d-tubocurarine in wax and peanut oil prolongs this action and offers another possible mode of treatment Evaluation of this type of therapy requires further study

In June of 1948 Berger and Schwartz[211] reported their studies on the oral use of a new drug '*myanesin*' (3-ortho-toloxy-1, 2 propanediol) in conditions associated with muscular spasm It had been used previously by parenteral injection but the effect then is of brief duration They administered the drug as a 3 3 per cent (weight in volume) solution in 20 per cent (volume in volume) aqueous propylene glycol with syrup of cherry 20 per cent (volume in volume) to improve the taste of the mixture The usual single dose was 30 c c equivalent to 1 0 gram of 'myanesin' Children were given proportionally smaller doses These investigators felt that administration of this remedy in tablet or capsule form did not always give satisfactory absorption of the drug Nevertheless it is now usually administered as tablets In parkinsonian syndrome the oral administration of 'myanesin resulted in diminution of tremor and rigidity More spectacular effects were seen after parenteral administration, but because of the brevity of action this mode of treatment did not seem practical Oral administration gave a much more prolonged action and did not cause side effects The best results were obtained if myanesin' was given in addition to the usual drugs of the atropine type described above Certain patients derived but little benefit from the medication More experience is needed in the evaluation of this treatment, but it offers additional help in the management of this distressing condition

These are the chief medicinal measures which have been found of some value in treatment of the nervous residuals of encephalitis Many cases resist all forms of therapy, and in others only partial or temporary

elief is secured. For this reason in the following section possible surgical measures of treatment are described.

Surgical Treatment of the Residuals of Encephalitis

Many residuals of encephalitis are so disabling and distressing that the patients welcome the trial of surgical procedures which may promise relief. Reports of operations undertaken for this purpose describe some degree of success. Bucy and Case[37] in 1939 reported relief of arm tremor resulting from traumatic injury by ablation of the contralateral arm area of the motor cortex. Klemme[23, 24] has reported a large number of cortical ablations for palsy, tremor and athetoid movements. In a series of 100 cases he reports that 39 patients were completely relieved and rehabilitated, 24 were relieved of signs and symptoms but some evidences of inertia were still present. Fourteen cases were relieved except for reappearance of tremor under excitement. Six cases were complete failures and there was an operative mortality of 17 per cent. Putnam succeeded in obtaining marked relief of unilateral tremor by section of the pyramidal tract at the level of the second cervical segment. The disability produced is less than that following cortical ablation in his opinion. Myerson and Berlin[26] have reported relief of postencephalitic parkinsonism after total ablation of the thyroid gland.

HERPES SIMPLEX ENCEPHALITIS

In the discussion of lethargic encephalitis it was noted that viruses which resemble or are identical with herpes virus have been isolated from a number of human cases of encephalitis considered to be of the lethargic type. According to Neal[161] this was done in 14 instances prior to 1934. This represented a very small percentage of positive results considering the large number of cases in which such isolation had been attempted. For that reason the theory that lethargic encephalitis is caused by herpes virus can not be considered to be established. There is however recent evidence that the virus of herpes can cause an encephalitis in man.

Smith, Lenette and Reams[162] in 1941 reported the isolation of herpes simplex virus from the brain of a fatal human case of encephalitis. They were able to demonstrate intranuclear inclusion bodies in the brain tissue

similar to those seen in herpes encephalitis in the rabbit A meningo-encephalitis with perivascular cellular infiltrations also was present

Two other more recent reports of herpes encephalitis are those of Zarafonetis Smadel Adams and Haymaker[163] in 1944 and Whitman Wall and Warren[161] in 1946 In the latter case the examination of the brain showed areas of softening associated with loss of ganglion cells which had been replaced by gitter cells Special staining technique was required to bring out the acidophilic intranuclear inclusions The original brain material yielded virus when inoculated into mice, guinea pigs and hamsters When inoculated into chick embryos, it produced pock formation on the chorio-allantoic membrane a phenomenon which the authors state is produced by no other neurotropic virus

Intranuclear inclusion bodies have not been a demonstrable finding in human lethargic encephalitis It is noteworthy that the inoculation of herpes virus into Cebus monkeys produces an encephalitis resembling the lethargic type in man Intranuclear inclusions are demonstrable in the early stages but not in the late stages of the disease in these animals[16] The cases of human encephalitis in which herpes virus and inclusion bodies have been demonstrated, have died in the acute stage of the disease

Herpes simplex encephalitis is now established as an infection which occurs in man Its relation to lethargic encephalitis remains uncertain

The causative agent of herpes simplex belongs to the viruses of the genus *Scelus* and has been given the designation *Scelus recurrens*[219] It is the common cause of fever blisters in man It has been transmitted successfully to rabbits guinea pigs white mice, cats, geese hedgehogs and the chick embryo It has a slight serological relationship to the virus of pseudo-rabies but none to vaccinia virus or to the known encephalitic viruses of the genus *Erro*[219]

No effective methods of prevention or treatment are available

POST-INFECTIOUS ENCEPHALITIS

A number of the acute infectious diseases of virus or bacterial origin occasionally are followed by encephalitis Influenza[166] measles[167] and German measles[168], mumps[169] variola[170] vaccinia[171] varicella[172], infectious mononucleosis[208] and pertussis[173 174] are all infections following which encephalitis has occurred While the seasonal incidence of these infec-

tions is somewhat variable they occur most commonly in the late fall winter and early spring

The encephalitis observed following these infections is characterized by a marked similarity in clinical symptoms and also in the pathological lesions produced in the nervous system There is no direct evidence that the viral agents which cause a number of these infections are operative in producing the encephalitis which follows although this possibility can not be ruled out Some believe that the antecedent acute infection may lower resistance to an as yet undiscovered neurotropic virus which is the actual cause of the encephalitis It is a curious fact that encephalitis following these infections other than influenza and perhaps mumps was mentioned seldom prior to 1918 suggesting that the occurrence of the pandemic of lethargic encephalitis possibly may have influenced the appearance of this form of encephalitis However the pathological picture seen in these cases differs from that of lethargic encephalitis Some regard post infectious encephalitis to be the result of a toxin or an allergic reaction to the infecting agent In the case of the nervous symptoms following whooping cough there is evidence that the hemorrhages in the brain following the violent paroxysms of coughing may be in part responsible

The pathological picture which is common to the entire group is characterized by congestion and multiple small hemorrhages and by the occurrence of perivascular areas of demyelination particularly in the white matter Perivascular lymphocytic infiltrations occur only occasionally and destruction of nerve cells is not a prominent feature Numerous vascular lesions are noted including swelling and hyperplasia of the endothelium and extensive thrombi These may account for some of the nervous symptoms[169, 174, 175, 176]

Some cases presenting this pathological picture have occurred without recognizable antecedent acute infections To these the designation of acute disseminated encephalomyelitis has been given Some of these cases may closely resemble multiple sclerosis[177, 178]

Post influenzal Encephalitis

The occurrence of cases presenting the clinical picture of encephalitis more or less in association with epidemics of influenza has been recorded for many years *During the influenza epidemic of 1889 1890* Pfuhl and Leichtenstern[6] described a type of hemorrhagic encephalitis

which they believed to be due to influenza Ebstein[9] about the same time described another group of cases to which the name, "nona", has been given These also had symptoms suggestive of infection of the central nervous system

In 1909 Hassin[1] described 4 cases of hemorrhagic encephalitis, 3 of which were preceded by an attack of influenza He states that most authors have found that some time elapses between the recovery from influenza and the onset of the symptoms of encephalitis This interval may be days, weeks and even months

Toward the end of World War I the pandemic disease which became known as 'lethargic encephalitis' made its appearance in Europe As already stated in this text, the first cases probably were observed in Rumania[3] in 1915 A number of additional cases occurred in France[4] in 1916 and in 1917 von Economo gave his classical description of this disease based on cases which he observed in Vienna during the winter of 1916-1917 In this first publication von Economo felt it necessary to raise the question whether these cases, which he was observing, could be cases of influenzal encephalitis He offers as evidence against this idea that there was no unusual prevalence of influenza in Vienna at the time, and that the pathological picture in the brain in cases of lethargic encephalitis did not show the hemorrhagic lesions described by Pfuhl and Leichtenstern The great influenza epidemic did not occur until at least a year later

In the United States lethargic encephalitis and the 1918 pandemic of influenza made their appearance about the same time However, the last wave of the pandemic of influenza was over by the spring of 1920, whereas the peak of the cases of lethargic encephalitis was not reached until the year 1923 and the disease continued with high prevalence for a number of years thereafter Hurst[180] made an extensive study of the statistics of the two diseases and came to the conclusion that there was no parallelism in the outbreaks of these two infections

In 1930 Greenfield[166] described an acute disseminated myelitis as a sequel to influenza The pathological lesions in the two cases, which he described, were characterized particularly by demyelination and resembled the findings in cases of encephalomyelitis which have followed vaccination smallpox and measles

Viruses known to be the causative agents of influenza have now been isolated[31] and occur in several serologically distinct types They cause pathological lesions when inoculated into ferrets, mice and

hamsters They can cultivated readily in eggs and have the property of agglutinating chicken erythrocytes [9]

Neal and Wilcox[10] in 1937 reported observations on a number of cases in which an acute respiratory infection diagnosed as grippe had been followed by development of various neurological conditions In 16 such instances the serum of the patients obtained from one to four months after the respiratory infection failed to show the presence of influenzal antibodies in 14 and only very weak antibodies in the other 2 cases

In 1945 Brown Muether Pinkerton and LeGier[11] reported observations on a case of encephalitis which followed a respiratory infection at a time when influenza was prevalent A high titre of influenza antibodies was found in this case Spinal fluid from this patient was inoculated into chicken eggs The chorioallantoic fluid of these eggs gave a weak positive agglutination to chicken erythrocytes This reaction became stronger in subseqent transfers After a number of transplantations in eggs the chorioallantoic fluid was inoculated intranasally and intracerebrally into mice with the production in a large percentage of animals of pneumonia and mild encephalitis Several successful mouse passages were made but later the virus was lost Serological tests of this virus by the antihemagglutinin test of Hirst [12] with known influenza virus antiserum type A and type B failed to indicate serological relationship with these strains of influenza virus The patient s own serum inhibited the agglutination of chicken cells by this agent in a dilution of 1/ 50 The identity of the infecting agent was not established and the possibility that it was a virus occurring spontaneously in mice can not be excluded During these studies it was noted that intracerebral injection of mice with the Pr 8 strain of influenza virus produced a mild encephalitis This fact has been reported also by Henle and Henle[13]

Proof of the existence of true influenza encephalitis in man can not been established until typical viruses of the influenza group are isolated from human brain material of a definite case of encephalitis This so far has not been accomplished

In addition to the question of the occurrence of cases of encephalitis caused by influenza virus there is also the possibility that an infection with the virus of influenza may lower the resistance of the body so as to allow invasion by some other virus with neurotropic properties Many believe in the existence of this relationship between influenza

which they believed to be due to influenza Ebstein[9] about the same time described another group of cases to which the name, "nona", has been given These also had symptoms suggestive of infection of the central nervous system

In 1909 Hassin[1] described 4 cases of hemorrhagic encephalitis, 3 of which were preceded by an attack of influenza He states that most authors have found that some time elapses between the recovery from influenza and the onset of the symptoms of encephalitis This interval may be days, weeks and even months

Toward the end of World War I the pandemic disease which became known as 'lethargic encephalitis' made its appearance in Europe As already stated in this text the first cases probably were observed in Rumania[3] in 1915 A number of additional cases occurred in France[4] in 1916, and in 1917 von Economo gave his classical description of this disease based on cases which he observed in Vienna during the winter of 1916 1917 In this first publication von Economo felt it necessary to raise the question whether these cases, which he was observing, could be cases of influenzal encephalitis He offers as evidence against this idea that there was no unusual prevalence of influenza in Vienna at the time, and that the pathological picture in the brain in cases of lethargic encephalitis did not show the hemorrhagic lesions described by Pfuhl and Leichtenstern The great influenza epidemic did not occur until at least a year later

In the United States lethargic encephalitis and the 1918 pandemic of influenza made their appearance about the same time However, the last wave of the pandemic of influenza was over by the spring of 1920 whereas the peak of the cases of lethargic encephalitis was not reached until the year 19.3 and the disease continued with high prevalence for a number of years thereafter Hurst[180] made an extensive study of the statistics of the two diseases and came to the conclusion that there was no parallelism in the outbreaks of these two infections

In 1930 Greenfield[168] described an acute disseminated myelitis as a sequel to influenza The pathological lesions in the two cases, which he described were characterized particularly by demyelination and resembled the findings in cases of encephalomyelitis which have followed vaccination smallpox and measles

Viruses known to be the causative agents of influenza have now been isolated[31] and occur in several serologically distinct types They cause pathological lesions when inoculated into ferrets, mice and

According to Ford[181] the mortality is about 10 per cent Nearly two thirds of those who survive show some residuals such as weakness in 30 per cent ataxia in 12 per cent mental and personality defect in 1 per cent and epilepsy in 5 per cent Neal and Harrington[171] observed a mortality of 13 5 per cent Of the survivors 73 per cent made complete recoveries Twenty seven per cent showed a variety of residuals of greater or lesser severity

Immune globulin which is of some value in measles so far has not been reported as of value in post measles encephalitis Unless this proves of some value treatment is entirely symptomatic

German Measles Encephalitis

Serious nervous symptoms following German measles were reported very rarely prior to 1934 Headache and rigidity of the neck frequently have been noted at the onset when lymph nodes at the base of the skull often become greatly enlarged After the year 1934 a number of cases of encephalitis following this infection were seen in various parts of the United States[1 3 4 4 186 1 7 188]

The clinical picture is marked by sudden onset of fever headache neck rigidity, drowsiness convulsions coma muscular tremor and at times ataxia The spinal fluid shows a variable cell count with lymphocytes usually predominating although Neal[171] has observed a case in which polymorphonuclears were in the majority The total number of reported cases is small and these include 5 fatal cases so that the mortality would appear high Little is known concerning residuals No specific treatment is available

Encephalitis Following Variola (Small Pox)

Encephalitis as a complication of variola (small pox) apparently is quite rare The most extensive studies of this condition have been published in England Rolleston[189] and Marsden and Hurst[176] describe an encephalomyelitis with onset usually between the fifth and thirteenth day after the appearance of the rash The chief symptoms are headache and drowsiness irritability and an unsteady gait Nausea and vomiting sometimes occurred with salivation and marked sweating Spinal and cranial nerves may be involved Rice and Carey[190] report a case from the United States with hemiplegia

and encephalitis who question the occurrence of encephalitis due to the influenza virus itself

Encephalitis Following Measles

Symptoms suggesting encephalitis probably occur more frequently following measles than any other of the common exanthemata of the childhood period. Typical cases of this condition have been reported more frequently in recent years than in the years prior to 1918. However the 1916 edition of Osler and McCrae's Text Book of Medicine[10] notes among the neurological complications of measles hemiplegia, paraplegia, acute mania, meningitis' and multiple sclerosis

Ford[184] notes that neurological complications occur in 0.4 per cent of all cases of measles. He distinguishes syndromes indicating diffuse cerebral involvement, multiple focal or diffuse lesions, single focal lesions, cerebellar syndromes, spinal syndromes and optic neuritis. Nervous symptoms make their appearance usually on the fourth to the sixth day of the course of measles after the rash has begun to fade. Occasionally, as in a case described by Malamud[185] the nervous symptoms may precede the appearance of the rash. Neal and Harrington[174] describe measles encephalitis as of sudden onset, accompanied by fever, headache and stiffness of the neck. Convulsions, vomiting and muscular twitching also are common symptoms. Usually the mental condition of the patient is somewhat disturbed, varying from mild irritability or apathy to marked drowsiness, stupor or delirium. Paralyses or pareses are seen involving cranial nerves or those of the trunk or extremities. Diplopia was observed in two instances. The paralyses may be spastic or flaccid. Superficial and deep reflexes were variable throughout the illness, more often diminished than hyperactive. About one half of the patients showed positive toe signs at some time during the course of the encephalitis. Inequality of pupils with sluggish reactions occasionally are observed. Temporary blindness sometimes occurs. The duration of the illness is quite variable, lasting from two weeks to several months.

Spinal fluid examination shows as a rule some increase in pressure with a slight rise in the cell count to levels usually less than 100 per cu mm, although in one instance a cell count of 540 was observed[174]. Lymphocytes and mononuclears predominate. Protein content is normal or slightly increased. Sugar is normal or high. The peripheral blood usually shows a moderate polymorphonuclear leucocytosis

Gordon[196] and McIntosh[197] believed that they were able to produce encephalitis by inoculation of vaccinia virus Iker[16] was not able to produce encephalitis unless the animal was subjected also to excessive heat or trauma Bouman[194] and Matsuda[199] could not produce encephalitis in animals by vaccinia virus inocluations The positive results were obtained many times in rabbits which are subject to spontaneous encephalitis after various experimental inoculations

Pathology

The pathology of post vaccinal encephalitis has been described by Turnbull and McIntosh[194] and by McIntosh and Scarff[19] They describe widely disseminated lesions both in the brain and the cord involving both the grey and white matter without any sharp localization of lesions Little meningeal involvement was noted Marked demyelinization was present with perivascular infiltrations spreading out into the surrounding parenchyma Some vessels showed hyalin thrombi with some endothelial proliferation Few hemorrhages were seen In the exudate were many large endothelial cells with clear oval nuclei together with a few lymphocytes and polymorphs Plasma cells were found rarely

Perdrau[0] in his study of the pathology of this condition also described the perivascular areas of demyelinization and expressed his belief in the histological identity of the lesions with those seen in the encephalitis following the Pasteur treatment of rabies following measles small pox *and other acute fevers as well as points of similarity to multiple* sclerosis Finley[191] also stresses the similarity between these types of encephalitis He pointed out the similarity also in the incubation period in these various forms of encephalitis averaging about 11 days

Onset and Clinical Course

Encephalitis following vaccination need not have been preceded by a severe reaction to the vaccination itself The neurological symptoms may appear as early as the 2nd and as late as the 25th day after the inoculation but with most cases the onset is between the ninth and fifteenth day The onset may be abrupt or gradual Convulsions are seen fairly commonly Somnolence apathy and stupor occur in most cases with some signs of meningeal irritation Some alteration of the deep reflexes with pathological toe signs often are observed Peripheral

Examination of the spinal fluid in the cases of Marsden and Hurst[176] showed a pleocytosis of from 10 to 500 cells per cu mm of which half may be granulocytes in the early stages of the encephalitis Later lymphocytes only were found A number of deaths occurred The pathology of this condition has been described by Finley[191] as well as by Marsden and Hurst[176]

Post Vaccinal Encephalitis

Prior to the appearance of the pandemic of lethargic encephalitis following World War I cases of encephalitis associated with vaccination against small pox very rarely were reported In the ten year period between 1924 and 1934 these cases became sufficiently numerous to attract attention Comby[192], Lucksch[192], Bastiaanse[193] and Turnbull and McIntosh[194] contributed to our knowledge of this condition There appears to have been a decline in cases of post-vaccinal encephalitis in recent years coincident with the decline in lethargic encephalitis

Several theories regarding the origin of this form of encephalitis have been offered

(1) That it is due to the vaccinia virus itself, this virus having developed neurotropic properties in such cases The increase coincident with the epidemic of lethargic encephalitis would in this case be explained by better recognition of all types of encephalitis due to the greater interest of physicians in this group of diseases at this time

(2) That some other neuroptropic virus was activated by the vaccinal infection, and a symbiotic action of the two viruses accounts for the encephalitis The neurotropic virus activated in this manner, might be a single agent and might even be the virus of lethargic encephalitis itself

(3) Post-vaccinal encephalitis may represent an allergic reaction to vaccination This theory would seem to infer that the cerebral vascular lesions may occur as a result of pathological changes analogous to the periarteritis nodosa which may follow serum injections Rivers[195] suggests that the vaccinal virus lesions in the skin might release antigens which would particularly affect other structures of ectodermal origin such as the brain

In regard to the direct causation of encephalitis by vaccine virus there are a number of studies in which the effect of intracerebral inoculations of this virus in animals was noted The results are quite variable

Gordon[196] and McIntosh[197] believed that they were able to produce encephalitis by inoculation of vaccinia virus Ikei[16] was not able to produce encephalitis unless the animal was subjected also to excessive heat or trauma Bouman[195] and Matsuda[199] could not produce encephalitis in animals by vaccinia virus inoculations The positive results were obtained many times in rabbits which are subject to spontaneous encephalitis after various experimental inoculations

Pathology

The pathology of post vaccinal encephalitis has been described by Turnbull and McIntosh[191] and by McIntosh and Scarff[19] They describe widely disseminated lesions both in the brain and the cord involving both the grey and white matter without any sharp localization of lesions Little meningeal involvement was noted Marked demyelinization was present with perivascular infiltrations spreading out into the surrounding parenchyma Some vessels showed hyalin thrombi with some endothelial proliferation Few hemorrhages were seen In the exudate were many large endothelial cells with clear oval nuclei together with a few lymphocytes and polymorphs Plasma cells were found rarely

Perdrau[200] in his study of the pathology of this condition also described the perivascular areas of demyelinization and expressed his belief in the histological identity of the lesions with those seen in the encephalitis following the Pasteur treatment of rabies following measles small pox and other acute fevers as well as points of similarity to multiple sclerosis Finley[191] also stresses the similarity between these types of encephalitis He pointed out the similarity also in the incubation period in these various forms of encephalitis averaging about 11 days

Onset and Clinical Course

Encephalitis following vaccination need not have been preceded by a severe reaction to the vaccination itself The neurological symptoms may appear as early as the nd and as late as the 5th day after the inoculation but with most cases the onset is between the ninth and fifteenth day The onset may be abrupt or gradual Convulsions are seen fairly commonly Somnolence apathy and stupor occur in most cases with some signs of meningeal irritation Some alteration of the deep reflexes with pathological toe signs often are observed Peripheral

muscle palsies occasionally occur together with muscle twitching and tremors Sensory changes are rare The spinal fluid may be normal, but frequently some increase in pressure and moderate pleocytosis are noted In general it is not easy to distinguish the clinical findings from those of epidemic encephalitis or the encephalitis following measles

Persistent nervous residuals occur in some cases Neal[1 1] describes as residuals nervousness stammering, muscular atrophy and contracture and lowered intelligence quotient These resemble the residuals of lethargic encephalitis

The mortality in this type of encephalitis has been between 30 per cent and 50 per cent

Since no specific *treatment* is known the management of each case is on a symptomatic basis

Encephalitis Following Chicken Pox

The older literature makes little reference to neurological complications following varicella Osler s 1916 edition of his Textbook of Medicine[10] mentions hemiplegia as a rare complication More recently case reports of encephalitis following this disease are appearing with increasing frequency Underwood[0] collected 119 cases from the literature up to 1935 with a mortality of 10 per cent and with the occurrence of chronic residuals in 12 6 per cent Bullowa and Wishik[13] reported that encephalitis occurred as a complication in 5 instances in -,534 cases of varicella seen between the years 19 9 and 1933 an incidence of 0 - per cent Neal[174] and Lowry[01] also have reported observations on this condition

The onset usually is two to eight days after the appearance of the rash and occurs suddenly Fever headache vomiting and stiffness of the neck are the most constant symptoms Somnolence apathy stupor or irritability were present in most cases Irregular changes in the deep and superficial reflexes were noted Strabismus nystagmus and blurring of vision occasionally occurred Hemiplegia and paralyses of the extremities occur rarely

The spinal fluid showed an increased cell count which was often above 500 per cu mm with mononuclear cells predominating The extremes of the counts noted were as low as 15 per cu mm to as high as 2 795 per cu mm In the case with the highest count 85 per cent of the cells seen were polymorphonuclears

The residuals noted are similar to those seen after encephalitis due to measles No preventive measures are available and there is no specific treatment

ENCEPHALITIS FOLLOWING MUMPS

The identification of the causative agent of mumps as a filterable virus was reported by Johnson and Goodpasture in 1934 The fact that neurological symptoms often are noted in association with this infection had been recorded at a much earlier date[10] Holden Eagles and Stevens[06] studied 100 consecutive cases of mumps admitted to the A S F Regional Hospital at Fort Benning Ga Of these 33 showed clinical signs of meningoencephalitis Ten additional cases were found to have changes in the spinal fluid pleocytosis and increased protein without clinical symptoms of involvement of the central nervous system The meningoencephalitis following mumps is believed by many to be due to the causative virus of mumps itself[16] Nevertheless as in the case of other postinfectious types of encephalitis the possibility that this virus infection merely lowers resistance against the invasion of some other neurotropic virus can not be excluded The author has seen a rising titre of virus neutralizing antibodies against the virus of St Louis encephalitis during the convalescent period of a case of encephalitis which developed during an attack of mumps

Kane Enders Cohen and Levens have developed a complement fixation test as an aid in the diagnosis of this condition They found that complement fixing antibodies appear 8 to 14 days after experimental inoculation in monkeys In a study of 51 cases of 'aseptic meningitis they noted complement fixing antibodies against mumps virus in approximately two thirds of their cases One third of their cases had had a recent attack of parotitis One third had antibodies against mumps virus without a previous history of an attack of mumps This suggests that mumps virus may possibly cause an aseptic meningitis in some cases without giving rise to parotitis

While mumps may appear at any season most outbreaks of this disease are noted between December and the end of June In the cases of aseptic meningitis studied by Kane and Enders[7] 94 per cent of those associated with parotitis occurred in the first seven months of the year Of the cases giving positive complement fixation tests without parotitis 73 per cent occurred in the first seven months of the year The cases

muscle palsies occasionally occur together with muscle twitching and tremors Sensory changes are rare The spinal fluid may be normal, but frequently some increase in pressure and moderate pleocytosis are noted In general it is not easy to distinguish the clinical findings from those of epidemic encephalitis or the encephalitis following measles

Persistent nervous residuals occur in some cases Neal[174] describes as residuals nervousness stammering muscular atrophy and contracture and lowered intelligence quotient These resemble the residuals of lethargic encephalitis

The mortality in this type of encephalitis has been between 30 per cent and 50 per cent

Since no specific *treatment* is known the management of each case is on a symptomatic basis

Encephalitis Following Chicken Pox

The older literature makes little reference to neurological complications following varicella Osler s 1916 edition of his Textbook of Medicine[10] mentions hemiplegia as a rare complication More recently case reports of encephalitis following this disease are appearing with increasing frequency Underwood collected 119 cases from the literature up to 1935 with a mortality of 10 per cent and with the occurrence of chronic residuals in 1. 6 per cent Bullowa and Wishik [13] reported that encephalitis occurred as a complication in 5 instances in 2,534 cases of varicella seen between the years 1929 and 1933 an incidence of 0 . per cent Neal[1 4] and Lowry [04] also have reported observations on this condition

The onset usually is two to eight days after the appearance of the rash and occurs suddenly Fever headache vomiting and stiffness of the neck are the most constant symptoms Somnolence apathy stupor or irritability were present in most cases Irregular changes in the deep and superficial reflexes were noted Strabismus nystagmus and blurring of vision occasionally occurred Hemiplegia and paralyses of the extremities occur rarely

The spinal fluid showed an increased cell count which was often above 500 per cu mm with mononuclear cells predominating The extremes of the counts noted were as low as 15 per cu mm to as high as . 795 per cu mm In the case with the highest count 85 per cent of the cells seen were polymorphonuclears

a preponderance of granulocytes but soon shifted to a picture of moderate leucocytosis and the differential showed a high percentage of lymphocytes and monocytes of the types seen commonly in infectious mononucleosis The titre of heterophile antibodies against sheep cells rose to 1 1250 The serum was tested also for neutralizing antibodies against St Louis encephalitis virus None were found during the convalescent period This patient made a rapid and complete recovery The examination of the spinal fluid during the height of the illness showed a normal cell count and no elevation of spinal fluid protein Several similar cases have been seen during the cooler months of the year when St Louis encephalitis was not prevalent A slight increase in lymphocytes in the spinal fluid was found sometimes as well as some increase in protein

Recent reports of the central nervous system symptoms of infectious mononucleosis are those of Gelebter[10] and Slade[11] The latter gives an excellent review of the literature and decribes the clinical features of this condition Fever headache somnolence and neck rigidity together with a slight lymphocytic pleocytosis in the spinal fluid are the most common findings The nervous manifestations are quite varied and evidences of spinal as well as meningeal and cerebral involvement may be seen

While most of the reported cases have recovered without serious residuals Slade[11] reports two cases in which the effects were sufficiently severe to require the permanent separation of soldiers from military service The author recently had an opportunity to see a case under the care of Dr W I Moore of St Louis in which respiratory paralysis occurred This has been the cause of death in at least four cases reported by Thomsen and Vimtrup[212] Ricker Blumberg Peters and Waderman[213] also have reported a fatal case due to ascending paralysis Like other types of post infectious encephalitis that accompanying mononucleosis may cause a fatal outcome in a disease usually considered to be quite benign

ENCEPHALITIS FOLLOWING WHOOPING COUGH

Convulsions occur quite frequently in whooping cough but are believed by Habel and Lucchesi[14] to be due to cerebral anoxia and hence do not necessarily indicate the presence of encephalitis Neal[214] has reported observations on 16 cases considered as having developed encephalitis as a complication of pertussis Convulsions somnolence stupor and apathy were common features in these cases Variable changes in

giving negative complement fixation tests for mumps virus mostly occurred in the warmer months of late summer and early autumn

The chief clinical symptoms of mumps meningoencephalitis[96] are headache, drowsiness and neck rigidity The leucocyte count in the peripheral blood varies between 4,000 and 1[illegible],000 per cu mm with the majority falling between 5,000 and 6,000 The spinal fluid cell count is somewhat elevated in nearly all cases and may be as high as 900 per cu mm The cells found are mostly lymphocytes Spinal fluid protein is elevated in about one fourth of all cases There is no relationship between the severity of the parotitis and the severity of the meningoencephalitis

Compared to other types of post infectious encephalitis such as those following measles rubella and varicella the symptoms usually are milder, chronic residuals are rare and the mortality is very low Osler and McCrae[10] state that the Index Catalogue of the Surgeon General's Office contains reports of 5 fatal cases up to 1916 A fatal case was reported by Larkin[163] in 19[illegible]0 The autopsy showed congestion of the pia arachnoid, slight distention of the ventricles and microscopically perivascular collections of large and small mononuclear cells in the pia arachnoid extending into the cortex

ENCEPHALITIS ACCOMPANYING INFECTIOUS MONONUCLEOSIS

The occurrence of symptoms of central nervous system involvement in cases of infectious mononucleosis has been recognized since the reports of Johansen[98] and of Epstein and Dameshek[99] in 1931 Since the cause of infectious mononucleosis remains obscure it is uncertain whether this is a virus infection of the nervous system It is also uncertain whether the nervous lesions are due to the causative agent of infectious mononucleosis or represent a complicating infection The onset of the nervous symptoms may precede or follow the appearance of the typical blood changes of this disease The author has had an opportunity to observe a number of cases suffering from this condition One case which began with a picture of encephalitis and raised a problem in differential diagnosis occurred in St Louis in August 1937 during the second epidemic of St Louis encephalitis A white female 20 years of age was taken ill suddenly with severe headache, a temperature of 104° F, drowsiness and marked neck rigidity The leucocyte count at the onset was low with

GROUP II

Types of Encephalitis Occurring Chiefly in Late Spring and Early Summer

RUSSIAN SPRING SUMMER TICK BORNE ENCEPHALITIS (FOREST SPRING ENCEPHALITIS)

Definition — Russian spring summer tick borne encephalitis may be defined as an acute infectious disease occurring in the late spring and early summer months caused by a filterable virus and transmitted by the bite of a tick characterized by lesions of the brain and spinal cord which frequently result in pareses and paralyses of the limbs neck and back with subsequent atrophy of the affected musculature

Historical Account

According to Smorodintseff [5] a clinical description of cases of this disease was given by Prof Pervushin of Perm about 1900 Cases were described in the Ural Mountains in 1914 and in the Far East in 1921 and 1923 The disease was intensively studied and its etiology and epidemiology clarified through the work of Olshenskaya Levkovich Silber Pavlovsky and Smorodintseff and their associates [1] during the years 1937 to 1939

Geographical Distribution

This form of encephalitis has been recognized in various parts of the U.S.S.R including the Far East Siberia the Ural Mountains and European Russia Beyond the limits of the Soviet Union it has not been described

Incidence

This type of encephalitis has a pronounced seasonal character Cases begin to appear by the end of April and gradually increase in number to reach a peak in the last ten days of May and the first ten days of June Seasonal temperatures usually are moderate and humidity is relatively high at this time of the year

the pupillary reactions and reflexes were noted The spinal fluid showed a slight to moderate lymphocytic pleocytosis This fluid was sometimes bloody At least one case developed chronic nervous residuals and there were 3 deaths in the series of 16 cases

Since whooping cough is considered to be of bacterial origin, we would have to consider the encephalitis to be a complicating infection if we wish to classify this type of encephalitis among those due to viruses

Considerable experimental evidence also incriminates the pasture tick as the vector of this disease Ticks collected from areas in which encephalitis is prevalent quite regularly can be shown to contain the encephalitis virus Intracerebral inoculation of mice with an emulsion of ground ticks causes the appearance of the picture of experimental encephalitis in these animals with a pathological picture similar to that of the human disease The virus isolated from the brains of these mice is serologically identical with strains of virus isolated in a similar manner from human autopsy brain material Negative results are secured from ticks collected in localities free of encephalitis Several species of pasture ticks are readily infected when fed on infected mice The virus persists for a long time in the body of the tick and in the case of *Ixodes persulcatus* it is transmitted from generation to generation of ticks Artificially infected ticks can transmit the disease also when they bite susceptible animals The virus in the tick apparently is transmitted to subsequent generations in the ova and survive the winter period Larvae hatched from ticks of infected areas are infected *Ixodes persulcatus* attacks men very actively and is the most common species of tick in the areas in which encephalitis is endemic However other ticks such as *Dermacentor silvarum* and *Haemophysalis concinna* may act also as vectors

Another virus reservoir lies in the wild animals of infected areas Encephalitis virus has been recovered from the bodies of a number of wild rodents in epidemic areas The infection in animals may be latent or apparent The disease therefore exists in nature independent of man

Etiology

Characteristics of the Virus – Like other viruses the causative agent of this disease is invisible on microscopic examination of infected material No inclusion bodies have been found on study of tissue sections The virus can not be cultivated in the absence of living cells It has been grown in tissue cultures of minced chick embryo in Tyrode solution with or without added rabbit serum It is readily filtered through Berkefeld or Chamberlain candles and is well preserved in glycerin

White mice monkeys goats sheep and many rodents are readily infected by the virus The experimental disease in monkeys is very similar to that in man Intracerebrally inoculated mice begin to show symptoms 4 to 10 days after injection They manifest irritability then

Children up to five years of age are seldom infected Young adult males are affected most frequently Old men and women are less susceptible to the disease

The disease occurs almost exclusively in uncultivated and slightly cultivated forest areas particularly in newly established communities Only those are affected who live and work in the woodlands or come in contact with them The great majority of cases occur in lumbermen, surveyors road-builders hunters geologists, etc

Epidemiology

There is little evidence of contact transmission The disease appears widely dispersed through vast forest areas at a time of the year when contact between the forest workers is limited Sick patients do not transmit the disease to others in their homes Cases treated in hospitals beyond the forest zone have not caused the appearance of the disease in the staff of any hospital although the virus has been found in the nose and throat and in the urine of encephalitis patients In the laboratory there is no evidence of spontaneous spread from animal to animal

Infection of human beings appears to be definitely linked with blood sucking vectors, namely the pasture ticks, *Ixodes persulcatus*, which in the act of biting introduces the neurotropic filterable virus in its saliva This statement is supported by the fact that most patients gave a definite history of having been bitten by a tick eight to eighteen days prior to the onset of the disease Practically all patients lived and worked in forests in which ticks are abundant The curve of the incidence of encephalitis parallels that of the tick population in nature Ticks appear prior to the onset of the first cases each year As the sexually mature forms of the pasture tick disappear, so also encephalitis vanishes from the population of the region The geographical distribution of the tick population coincides with that of the cases of encephalitis Forest areas, in which ticks are found rarely do not show cases of this disease There is evidence of immunity produced by frequent tick bites in areas in which infected ticks occur and in which the population has been long in residence The resistance of such individuals can be accounted for by the presence in their blood of virus neutralizing antibodies Similar changes are found in the blood of the domestic and wild animals in the same areas this being true of horses cows rodents and other wild animals

Considerable experimental evidence also incriminates the pasture tick as the vector of this disease Ticks collected from areas in which encephalitis is prevalent quite regularly can be shown to contain the encephalitis virus Intracerebral inoculation of mice with an emulsion of ground ticks causes the appearance of the picture of experimental encephalitis in these animals with a pathological picture similar to that of the human disease The virus isolated from the brains of these mice is serologically identical with strains of virus isolated in a similar manner from human autopsy brain material Negative results are secured from ticks collected in localities free of encephalitis Several species of pasture ticks are readily infected when fed on infected mice The virus persists for a long time in the body of the tick and in the case of *Ixodes persulcatus* it is transmitted from generation to generation of ticks Artificially infected ticks can transmit the disease also when they bite susceptible animals The virus in the tick apparently is transmitted to subsequent generations in the ova and survive the winter period Larvae hatched from ticks of infected areas are infected *Ixodes persulcatus* attacks men very actively and is the most common species of tick in the areas in which encephalitis is endemic However other ticks such as *Dermacentor silvarum* and *Haemophysalis concinna* may act also as vectors

Another virus reservoir lies in the wild animals of infected areas Encephalitis virus has been recovered from the bodies of a number of wild rodents in epidemic areas The infection in animals may be latent or apparent The disease therefore exists in nature independent of man

Etiology

Characteristics of the Virus — Like other viruses the causative agent of this disease is invisible on microscopic examination of infected material No inclusion bodies have been found on study of tissue sections The virus can not be cultivated in the absence of living cells It has been grown in tissue cultures of minced chick embryo in Tyrode solution with or without added rabbit serum It is readily filtered through Berkefeld or Chamberlain candles and is well preserved in glycerin

White mice monkeys goats sheep and many rodents are readily infected by the virus The experimental disease in monkeys is very similar to that in man Intracerebrally inoculated mice begin to show symptoms 4 to 10 days after injection They manifest irritability then

somnolence, convulsions and muscle palsies Death occurs in 6 to 24 hours after symptoms appear Mice are most susceptible by intracerebral inoculation less so to intranasal, subcutaneous and intravenous administration

This virus belongs to the genus *Erro* and has been given the specific name *Erro silvestris*[19]

According to the observations of Smorodintseff [15] the strains of this virus so far isolated appear serologically identical It differs from St Louis encephalitis virus both in antigenic and immunogenic properties there being no cross neutralization or immunity It is more closely related to Japanese B encephalitis Immune rabbit serum specific for Japanese B virus will partially neutralize Russian spring and summer encephalitis virus but not as completely as it neutralizes the Japanese B virus Antiserum against spring-summer encephalitis will also show activity against Japanese B virus Animals immunized against spring summer virus are also immune against Japanese B virus but those immune to B virus are not always immune to the Russian spring-summer virus

Casals [16] obtained somewhat different results He found that Russian encephalitis and louping ill viruses showed a close relationship by complement fixation neutralization and intraperitoneal cross resistance tests Intracerebral cross-resistance tests, on the other hand failed to reveal any connection between them Neither Russian encephalitis nor louping ill showed any relationship to Japanese B virus St Louis encephalitis or West Nile encephalitis In agreement with Casals Sabin[141] found no serological relationship between Russian spring-summer encephalitis virus and a strain of Japanese B virus which he isolated on Okinawa in 1945 There is therefore some contradiction in the serological relationship of these viruses in the reports so far available

Silber and Shubladze[217] report certain differences between the tick-born encephalitis viruses isolated in Western European Russia and strains isolated in Far Eastern Siberia The Western strains they found to be serologically identical with louping ill virus in agreement with the findings of Casals [16] The Far Eastern strains were serologically different and cause somewhat different symptoms when inoculated into sheep The Western virus is transmitted by *Ixodes ricinus*, whereas the Far Eastern strain is transmitted by *Ixodes persulcatus*

According to Warren[146] encephalitis cases occurring in the autumn in Far Eastern Siberia are identical with Japanese B encephalitis

According to the Russian observers virus neutralizing antibodies appear in the serum of infected human beings rather slowly Only about 10 per cent show antibodies before the 15th day after the onset By the 20th to the 30th day about 50 per cent show the presence of virus neutralizing antibodies After this nearly all cases show antibodies and once they appear they usually persist for many years There appears to be no parallelism between the level of serum antibodies and the gravity of the disease

Pathology

In Russian spring summer encephalitis severe inflammatory and degenerative changes are found not only in the brain and spinal cord but also in the sympathetic nervous system and the peripheral nerves The pathological picture is that of an acute non suppurative meningo encephalo polio myelitis The meninges show an acute serous meningitis The brain is congested and shows numerous hemorrhages in the brain stem the medulla and the horns of the spinal cord The lesions are perhaps most marked in the medulla and the grey matter of the spinal cord whereas in the cerebral cortex the changes are relatively slight Microscopically the lesions show perivascular infiltrations of the blood vessels of the grey and white matter and the meninges and also diffuse focal infiltrations of the grey matter with inflammatory cells These cellular infiltrations consist mostly of lymphocytes with a small number of polymorphonuclear leucocytes and glial cells The ganglion cells of the medulla and cord show various degenerative changes from slight chromatolysis and loss of Nissl granulation to complete neuronophagia Hemorrhages in the grey matter are seen quite frequently varying greatly in size and number[21]

Clinical Course

The incubation period is between 8 and 18 days The onset is marked by a rise in temperature to 38 to 40 C. The patient complains of severe headache pain in the muscles of the neck vertigo and vomiting[1]

Weakness and paralysis of the muscles of the neck and shoulder girdle develop usually by the second or third day of the disease drooping neck being a common symptom In unfavorable cases the lesions

ascend from the cervical cord to involve the basal ganglia of the brain with the appearance of grave bulbar symptoms Disturbances in respiration, disturbed cardiac activity and difficulty in swallowing and phonation may be seen Death often occurs suddenly between the 3rd and 8th day of the disease

The mortality is about 30 per cent, varying somewhat in different outbreaks

Convalescents frequently show persisting weakness, paralysis and atrophy of cervical muscles and the muscles of the shoulder girdle The Parkinsonian syndrome which is a frequent sequel of lethargic encephalitis, apparently does not occur in this disease

Differential Diagnosis

Russian spring-summer encephalitis differs from other types in its seasonal incidence which is highest in April, May and June This should be contrasted with lethargic encephalitis which occurs chiefly in the winter and early spring Also it differs from Japanese B encephalitis, St Louis encephalitis Eastern and Western equine encephalomyelitis and poliomyelitis, all of which occur in the late summer and early autumn

Spring summer encephalitis is limited to tick-infested forest areas whereas lethargic encephalitis is as common in the cities as in the country The late summer and autumn types such as Japanese type B and St Louis encephalitis have involved urban areas, but in the case of the St Louis epidemics the case incidence was higher in suburban and semi-rural portions of St Louis County than in the city Equine encephalomyelitis has been found most commonly in rural areas In none of these are heavily forested areas involved nor has association with ticks been a prominent feature Experimentally, it is true that St Louis encephalitis can be conveyed to animals by tick bites but this is not believed to be the common mode of transmission to man[230]

Spring and early-summer encephalitis appears to affect mostly young adults This age incidence is somewhat similar to that of lethargic encephalitis but differs from St Louis encephalitis and Japanese type B which in most outbreaks have their highest incidence in the older age groups Poliomyelitis has its greatest incidence in young children

Russian spring summer encephalitis frequently causes paralysis of the muscles of the neck and shoulder girdle a picture rarely seen in other types of encephalitis Parkinsonism is seen rarely in Russian encephalitis although a common sequel of lethargic encephalitis Permanent weakness and atrophy of the muscles of the shoulder girdle and neck is a common sequel of Russian encephalitis but rarely seen in other types

The differences in the serological reactions have been discussed already

Preventive Measures

Since ticks play an all important role in the transmission of spring summer encephalitis measures to protect human beings from these insects are important in the control of this disease Individuals working in forest areas should be examined regularly for the presence of ticks and when found these insects should be removed immediately and destroyed It can be shown in experimental animals that the length of the period during which the tick feeds on the animal is very important in the transmission of the disease In mice blood sucking for two to four hours will not transmit the disease whereas feeding for two to four days will cause infection[213] Examination of forest workers twice daily for ticks will greatly reduce the chance of infection Protective clothing is of value and the Russians have devised clothing of this type Garments impregnated with insect repellants are also useful Protection of camp sites by burning grass and spraying with insect repellants has been shown to be effective Finally efforts should be made to exterminate the wild rodents which serve as reservoirs of the infection

A protective vaccine has been prepared by Smorodintseff Kagan and Levkovich[215] from emulsions of infected mouse brain in which the virus has been killed by incubation with 1/600 to 1/750 formaldehyde for 15 to 20 days at 2 to 5 C Such a vaccine preserves its antigenic properties for about two months This vaccine caused no unfavorable reactions In a controlled study of its use it reduced the incidence of encephalitis to one tenth that of the control group and reduced the mortality to one third that of the controls Casals and Olitsky[21] also have prepared formalin inactivated Russian spring summer encephalitis virus vaccines which produced lasting immunity in mice

Treatment

Russian investigators have used both human convalescent serum and immune horse serum in the experimental and clinical treatment of this infection. To be effective it must be administered on the first or second day after the onset. It may be administered both intramuscularly and intraspinally. Oxygen inhalation apparently is of some value in treatment. The Russians also use urotropin and believe it to be of some value. They admit that serum treatment does not guarantee the patient against serious complications or even death and that further study of a satisfactory method of treatment is needed.[15]

GROUP III

Types of Encephalitis With Time of Onset Chiefly But Not Exclusively in the Late Summer And Autumn

EPIDEMIC SUMMER ENCEPHALITIS ST LOUIS TYPE

Definition —An acute infectious disease caused by a filterable virus characterized by non purulent inflammation of the brain with congestion and perivascular infiltration of lymphocytic and mononuclear cells The clinical picture includes a high but irregular fever accompanied by severe headache and by signs of meningeal irritation, usually somnolence and at times delirium and coma Non fatal cases terminate after a course of one to three weeks Serious chronic nervous residuals are rare

Historical Account

The first definitely recognized outbreak of this disease occurred in Paris Illinois between July and September 193 While the total number of cases was small the incidence per 100 000 population and the mortality were both higher than in any of the subsequent epidemics One year later a second epidemic occurred in the vicinity of St Louis Missouri This epidemic while most intense in St Louis City and County spread across the Mississippi river to involve neighboring communities in Illinois and also was known to have appeared in Columbia Kansas City and St Joseph Missouri and in Louisville Kentucky[17] An examination of the mortality statistics of the United States census for this year shows that deaths from encephalitis in this year exhibit a curious preponderance of summer over winter deaths in a large number of states

A white male 17 years of age whose illness began July 5 1933 with fever chills and headache was treated at Firmin Desloge Hospital in St Louis from the seventeenth to the twenty first of July The cell count of the spinal fluid was elevated and the neurological findings were considered by Dr L B Alford to be suggestive of encephalitis Subsequently virus neutralization tests showed that this case probably was a case of true St Louis encephalitis This individual was a resident of

Treatment

Russian investigators have used both human convalescent serum and immune horse serum in the experimental and clinical treatment of this infection To be effective it must be administered on the first or second day after the onset It may be administered both intramuscularly and intraspinally Oxygen inhalation apparently is of some value in treatment The Russians also use urotropin and believe it to be of some value They admit that serum treatment does not guarantee the patient against serious complications or even death and that further study of a satisfactory method of treatment is needed [1]

GROUP III

Types of Encephalitis With Time of Onset Chiefly But Not Exclusively in the Late Summer And Autumn

EPIDEMIC SUMMER ENCEPHALITIS ST LOUIS TYPE

Definition —An acute infectious disease caused by a filterable virus characterized by non purulent inflammation of the brain with conges tion and perivascular infiltration of lymphocytic and mononuclear cells The clinical picture includes a high but irregular fever accompanied by severe headache and by signs of meningeal irritation usually somnolence and at times delirium and coma Non fatal cases terminate after a course of one to three weeks Serious chronic nervous residuals are rare

Historical Account

The first definitely recognized outbreak of this disease occurred in *Paris Illinois between July and September 193 While the total num* ber of cases was small the incidence per 100 000 population and the mortality were both higher than in any of the subsequent epidemics One year later a second epidemic occurred in the vicinity of St Louis Missouri This epidemic while most intense in St Louis City and County spread across the Mississippi river to involve neighboring com munities in Illinois and also was known to have appeared in Columbia Kansas City and St Joseph Missouri and in Louisville Kentucky[17] An examination of the mortality statistics of the United States census for this year shows that deaths from encephalitis in this year exhibit a curious *preponderance of summer over winter deaths in a large number of states*

A white male 17 years of age whose illness began July 5 1933 with fever chills and headache was treated at Firmin Desloge Hospital *in St Louis from the seventeenth to the twenty first of July The cell* count of the spinal fluid was elevated and the neurological findings were considered by Dr L B Alford to be suggestive of encephalitis Sub sequently virus neutralization tests showed that this case probably was a case of true St Louis encephalitis This individual was a resident of

the west central part of the city of St Louis but near the border of the city and county The greater number of the earlier cases of the epidemic occurred in St Louis County and were treated and diagnosed at St Louis County Hospital The epidemic nature of the outbreak was recognized by the staff of the Health Division of the City of St Louis on August 8th Reported cases reached their maximum in St Louis County the week of September 2nd and in the city the week of September 16 The disease had practically disappeared in the county by the week of October 21 and in the city the week of November 11 The disease therefore appeared in epidemic proportions first in the county and reached its maximum and subsided at an earlier date in the county than in the city When studied regarding the day of onset of illness more city cases had their date of onset on August 27 than on any other day[17] The seasonal occurrence noted in the vicinity of St Louis was very similar to that seen in all areas in which the presence of this disease was recognized

After the epidemic of 1933 the disease apparently disappeared in the vicinity of St Louis except for a few doubtful sporadic cases until the summer of 1937 when a second outbreak occurred of about two thirds the proportions of the first epidemic[8] The seasonal incidence and spread of this outbreak was quite similar to that of the epidemic of 1933 Since this time St Louis encephalitis has been recognized in various parts of the United States[44, 101, 138, 139, 212, 243]

Geographical Distribution

The local geographical distribution of cases in both outbreaks in relation to population is extremely interesting The case incidence per 100 000 population in 1933 was 69 in the city of St Louis 212 in St Louis County In the city the oldest and most densely populated areas had a lower incidence rate than those newer sections of the city which bordered on St Louis County A more detailed analysis of case distribution has been made by Casey and Broun[83] In this study the area of the city and county was divided off into circular zones one mile in diameter The case incidence of encephalitis in each circular area was compared with the population density of the same area In this way it was possible to determine exactly what areas showed a case incidence greater than would be expected from the population density This study

showed that the areas where encephalitis was prevalent out of proportion to that which would be expected from the population density were all situated within one mile and all except one within one half mile of the small streams in St Louis and St Louis County The streams all or nearly all carried sewage The survey revealed a fairly close correlation between the occurrence of epidemic encephalitis foci and lack of outdoor sanitation in an area as judged by the presence of weeds open sewage ponds streams garbage and tincan dumps Ninety five per cent of the inhabited wood open sewage stream and pond areas of St Louis showed a significant (P 0 01) or probably significant (0 0 005 0 01) preponderance of encephalitis and 87 per cent of all cases occurred within a mile of such an area Every district in the St Louis area which was without weeds open sewage and ponds and which was separated a mile or more from such an area was not only without heavy concentrations of encephalitic cases but actually showed a statistically significant scarcity of encephalitis About 4 per cent of the population of St Louis lived under these fortunate conditions The prevalence of encephalitis in sewage stream pond and weed areas could not be explained on the presence of more old people in these areas as a control study was made regarding this point Nor could poverty and poor indoor sanitation explain it since the areas of greatest poverty and most unsatisfactory indoor sanitation had the least encephalitis in the St Louis area On the other hand foci did occur in districts where the inhabitants were wealthy and above average in wealth where these areas were within one half mile of streams and ponds and open sewers The disease did not tend to predominate in the more congested areas but actually predominated in the most sparsely settled areas of the city and county

Regarding the types of dwellings in which cases of encephalitis occurred a survey of 133 cases showed that 111 lived in single houses 10 in flats and 12 in apartments This again indicates that most cases were not from the most crowded districts About 15 per cent of cases reported known contact with other cases of encephalitis In less than 10 per cent of cases more than one case occurred in the same family In many households the least mobile member and the one least in contact with the outside world e g an individual bed ridden from chronic illness was the one stricken[17]

All of these features differ from diseases known to be spread by contact They are all identical with facts known about diseases which might

be spread by mosquitoes or other insect vectors The present status of knowledge regarding the possibility of mosquito transmission will be discussed presently

Climactic Conditions

Both the 1933 and 1937 outbreaks of encephalitis occurred during a period of drought and intense heat During June, July and August of 1933 according to official weather bureau records, the rainfall in St Louis and St Louis County was the lowest in its history up to that date The drainage and sewage disposal was favorable to the breeding of unusually large numbers of mosquitoes in areas commonly infested With the dry season the flow in these open ditches was very small and practically consisted of sewage only and odors that emanated from these places were quite offensive[17] In 1937 while the rainfall in June was somewhat more abundant August was both hot and dry Mosquitoes were again present in great numbers

It is of interest to note that the epidemics of Japanese summer encephalitis also occur during periods of drought and intense heat

However before too much stress be laid on climatic conditions the fact must be recorded also that during the hottest and driest of all summers in the St Louis area that of 1936, the disease did not reappear in an incidence sufficient for recognition In this summer it is true that the small streams and ponds were mostly completely dried up and the summer was not marked by the prevalence of great numbers of mosquitoes and other insects

Age and Sex Incidence

In both epidemics the disease occurred in all age groups but showed a definitely higher incidence in the higher age groups more so than in almost any other known infection except Japanese encephalitis[17] (see Table III) The mortality also is higher with advancing years

The sex incidence was practically identical with the sex distribution of the population 50 9 per cent males 49 1 per cent females The colored race numbering about 10 per cent of the population, had slightly less than 10 per cent of all cases[17]

Mortality

The mortality of reported cases of St Louis encephalitis during the epidemic of 1933 was 18 7 per cent The recurrence of 1937 showed in the city of St Louis a death rate of 4 8 per cent In both outbreaks the increased mortality with advancing years was seen clearly In addition the mortality of cases which had definite hypertensive vascular disease during the attack of encephalitis was quite high in all age groups In a series of 1 9 cases treated at Firmin Desloge Hospital in 1933 3- cases

TABLE III

Age Incidence of Neurotropic Virus Diseases

Age Period	*Encephalitis Lethargica*	*St Louis Encephalitis*	*Lymphocytic Choriomeningitis*	*Eastern Equine Encephalomyelitis*	*Western Equine Encephalomyelitis*	*Poliomyelitis*
0- 9	75 cases (16 2%)	28 cases (8 4)	8 cases (7 4%)	5 cases (65 %)	8 cases (2 2%)	(81%)
10-19	108 cases (23 4)	4 cases (7 2)	10 cases (9 3)	2 cases (25.0%)		(12%)
20-29	107 cases (23 2)	33 cases (9 9)	30 cases ([illegible])			(4%)
30-39	6? cases (14 3)	30 cases (9.0)	31 cases (28 7%)		25 cases (69.4%)	
40-49	53 cases (11 4)	41 cases (12 3)	18 cases (16)	1 case (12 5%)		(3%)
50 and above	53 cases (11 4)	178 cases (53 2)	11 cases (10 2%)		3 cases (8.4%)	

had hypertension In this hypertensive group the mortality was 31 per cent whereas the entire group had a mortality of only 12 3 per cent[98] Very young children show a higher mortality than those in the other lower decades

Etiology and Epidemiology

The majority of the studies of the etiology of St Louis encephalitis have failed to reveal evidence of the presence of bacteria in the brain

tissues except in cases with secondary infections[17] Rosenow[84] reported isolation of streptococci in cases which he studied For a full discussion of the evidences regarding bacteria as a causative factor the report of the St Louis outbreak of encephalitis, published by the Public Health Service, should be consulted[17]

The disease was transmitted successfully to macacus rhesus monkeys by Muckenfuss Armstrong and McCordock[8] by intracerebral inoculation with brain material secured at autopsy from human cases of encephalitis Many monkeys were however, resistant to the infection, and it was found difficult to insure perpetuation of the infection in this animal

Webster and Fite[86] using brain material preserved in glycerin, transmitted the disease to white mice and in this animal secured uniformally fatal results with definite doses of brain material They established the fact that the agent was filterable and hence presumably a virus They also showed that the convalescent serum of cases of St Louis encephalitis would neutralize this virus and protect inoculated animals from otherwise fatal doses This test has been extremely valuable in subsequent studies of this infection

The virus which they isolated is now generally accepted as the causative agent of St Louis encephalitis It has been classified as belonging to the viruses of the genus *Erro* and has been designated *Erro selestus*[19]

Later Muckenfuss, Armstrong and McCordock transmitted the virus from previously infected monkeys to mice[17] Broun Muether and Collier[9] established two strains of the virus in mice from human brain material, which had been preserved nearly three months in glycerin Greutter Broun and Muether isolated the virus from human brain material in the 1037 outbreak in St Louis proving the identity of the infection in this year with that of 1933[8]

Webster and Fite[88] have reported that serum of convalescents from Japanese encephalitis does not neutralize the St Louis virus, thus establishing a serological difference between these clinically highly similar infections Sera of patients convalescent from the von Economo type of lethargic encephalitis fail to show neutralizing antibodies against the St Louis virus indicating a serological difference between these two diseases[89]

Mice can be inoculated successfully with the virus by intranasal as well as intracranial inoculation Subcutaneous and intraperitoneal inocu

lations fail to produce encephalitis unless the brain has been injured previously When the virus is given subcutaneously, it acts as a vaccine protecting mice against subsequent intracranial inoculation for a period beginning 4 to 7 days after the injection and usually lasting about 8 weeks[90] A curious fact, noted by Webster, is that during the period of cerebral immunity following subcutaneous vaccination the serum of the mice contains no virus neutralizing antibodies When the cerebral immunity is lost, virus neutralizing antibodies appear in the serum[91]

The ease with which white mice can be infected with the virus of St Louis encephalitis naturally led to interest in wild mice as a possible source of infection At least three varieties of wild mice have now been shown to be highly susceptible to infection by this virus Harford Sulkin and Bronfenbrenner[95] showed that the house mouse *Mus musculus* can be infected Greutter Fulton Muether Hanss and Brown[96] have demonstrated that the field mouse *Reithrodontomys megalotis*, and the meadow mouse *Microtus ochrogaster* are susceptible also All three of these types of mice are common in the vicinity of St Louis Mice trapped in the homes of encephalitic patients to the present time have not been found to be carriers of the virus While mice therefore are a potential source of infection they have not been shown to be involved in the causation of the epidemics so far studied

The successful transmission of St Louis encephalitis to the hamster was reported by Brown Muether Mezera and LeGier[97] in 1941 This provided investigators of this disease with a readily available susceptible laboratory animal of larger size than the mouse for serological studies[98]

The question of a gastrointestinal portal of entry has been raised by the work of Harford Sulkin and Bronfenbrenner[92] Ordinarily it is rather difficult to infect animals by this route and there is question whether contamination of the nasal mucosa does not occur during ingestion of the infected material Mezera[99] has shown that administration of St Louis encephalitis virus by mouth to hamsters is followed by the appearance of virus neutralizing antibodies in the blood although no obvious illness is produced

The possibility of mosquito transmission of the virus of St Louis encephalitis was studied during and following the epidemic of 1933 Mosquitoes were allowed to bite volunteer convicts in the state penitentiary after biting cases of encephalitis These experiments gave uniformly negative results[17]

Later Webster Clow and Bauer[93] working with anopheles mosquitoes showed that the virus is taken into the body of the mosquito from

infected mice and survives for a period as long as 28 days, even increasing in amount during this time However, allowing the infected mosquito to bite another mouse did not give rise to disease in that animal As mentioned above subcutaneous injections of virus usually are ineffective in securing infection of the brain in animals inoculated by this route

Fulton Greutter Muether, Hanss and Broun[91] reported similar results in experiments in which *Culex pipiens*, secured from the St Louis area were allowed to bite mice heavily infected with the virus of St Louis encephalitis The virus could be demonstrated in the body of this mosquito after biting an infected animal but subsequently, when these mosquitoes bit another animal, in no case did these develop encephalitis Adult mice were used in these experiments Other investigators subsequently showed that use of newborn mice greatly facilitated transmission experiments of this type

Blattner and Heys[30] have shown that St Louis encephalitis may be transmitted to young mice by the bite of ticks The location and distribution of cases as well as the individual histories obtained from patients during the St Louis epidemics of 1933 and 1937 do not suggest a tick borne disease These experiments, however, indicate the possibility of this mode of spread in certain cases They have isolated the virus of St Louis encephalitis from the blood of a human case[31]

In 1934 Broun Muether and Collier[87] reported that a high percentage of the cases of St Louis encephalitis observed in the epidemic of 1933, had had close contact with chickens In 1941 Hammon, Gray, Evans and Izumi[3] reported the presence of virus neutralizing antibodies against St Louis encephalitis virus in the sera of wild and domestic mammals and birds studied in the Yakima Valley of Washington where an epidemic of this disease occurred Of the sera of 77 domestic mammals studied 37 per cent protected against the St Louis virus in contrast to 9 per cent of 65 wild animals More striking still were the findings in the sera of chickens and other domestic birds where 50 per cent showed protection against St Louis virus compared to 15 per cent of 87 wild birds These findings were significant in that they indicated domestic fowls and animals could serve as a potential reservoir for the St Louis virus They found that the distribution of cases in the Yakima Valley supported this supposition, namely that domestic fowl may have served as the source of the infection Further studies by Hammon and Reeves[33] disclosed the presence of St Louis encephalitis virus in mosquitoes of the species *Culex tarsalis* captured in the Yakima Valley While guinea pigs

cats and horses showed no viremia after inoculation with St Louis encephalitis virus birds particularly chickens ducks and doves developed viremia Subcutaneous inoculation of 0 cc of the dilution of virus which killed 50 per cent of mice when 0 03 cc was inoculated intracerebrally produced viremia in 5 of 6 chickens Furthermore the virus multiplied in the chickens to such an extent that tenfold and occasionally hundredfold dilutions were infectious for mice These experiments showed that the mosquito might acquire the virus by biting infected chickens and then transmit the virus to other chickens ducks and doves The infected fowl show no obvious illness[?] Subsequent studies have shown that many species of mosquitoes may transmit encephalitis virus These are *Culex tarsalis Culex pipiens Culex coronator, Anopheles lateralis Anopheles nigromaculis Culex incidens* and *Culex mornata* Survival of the virus but no transmission occurred in *Culex quinquefasciatus Culex stigmatosoma Psorophora ciliata* and *Anopheles maculopennis Freeborni* These investigations indicate that fowl may serve as a reservoir of St Louis virus in nature and that mosquitoes may serve as the vector by which the disease is transmitted from fowl to man[?]

Another link in the chain of the epidemiology of St Louis encephalitis was furnished by the studies of Smith Blattner and Heys[?] in 1944 They reported the isolation of St Louis encephalitis virus from chicken mites *Dermanyssus gallinae* found on chickens in the vicinity of St Louis The sera of these chickens showed the presence of antibodies against St Louis encephalitis The mites not only were shown to carry the virus but to pass it from generation to generation in the process of breeding While these mites are not believed to bite man it is believed that they maintain the infection in chickens of an endemic area and when circumstances are favorable an epidemic may arise from such a focus The present conception would make the actual transfer of infection from fowl to man take place by mosquito transmission

The pathology of this disease has been described carefully by McCordack and Collier[11] The essential pathological process is an acute nonpurulent inflammation of the central nervous system characterized by intense vascular congestion with petechial hemorrhages cellular infiltration of both nervous tissue and meninges with various types of mononuclear cells and evidences of toxic degeneration in the nerve cells

On opening the meninges it was noted that the amount of cerebrospinal fluid was increased in most cases where it had not been drained recently by lumbar puncture Every brain examined showed grossly

obvious congestion of meningeal and intracerebral vessels often with minute hemorrhages The cut surface often showed a light, salmon pink color due to intense capillary congestion This was sometimes diffuse more often blotchy in distribution Increased softness of the brain tissue, due to edema was encountered often

Pathology

The chief changes found in the nervous system on microscopic examination were vascular congestion and hemorrhages cellular infiltrations and nerve cell degeneration The vascular congestion was widespread and involved vessels of all sizes down to capillaries Cellular infiltrations of three types were noted (1) perivascular cuffs around the blood vessels consisting chiefly of lymphocytes but with occasional mononuclear and a few polymorphonuclear cells, (2) scattered foci in the brain tissue, not in connection with blood vessels of mononuclear cells some being lymphocytes and others probably of glial origin Degenerated nerve cells were seen sometimes in these foci (3) diffuse cellular infiltrations of the brain tissue sometimes slight and sometimes very marked

The meninges while never showing a frank exudate showed microscopic infiltrations of mononuclear cells in some three fourths of all cases examined In one fourth of the cases these infiltrations were well marked These infiltrating cells were chiefly lymphocytes and plasma cells with, occasionally, large mononuclear phagocytes and rarely a few polymorphonuclear leucocytes Pathological changes in nerve cells of varying degree and distribution were found in practically all cases Perinuclear chromatolysis eccentric nucleus swollen nucleolus and excess of pigment were seen commonly Shrinkage of nerve cell body with pycnotic nuclei and darkly staining or practically liquefied cytoplasm was seen in cases showing extensive cellular infiltrations

Amyloid bodies sometimes described as occurring in young individuals with lethargic encephalitis were seen chiefly in aged individuals with the St Louis type Perivascular patches of demyelination, considered to be quite characteristic of post vaccinal and post measles encephalitis were never found

Examination of the proximal ends of the cranial nerves showed only slight changes in these chiefly in the optic and trigeminal nerves

The congestion and minute hemorrhages occurred diffusely throughout the brain and cord. Cellular infiltrations in some cases with intense reaction occurred in all parts of the brain, in others they were limited to the pons, more often to pons, mid brain, basal nuclei and white matter of the cerebrum. Nerve cell degeneration, while often seen in the cortex, was more frequent in the pons, basal nuclei and medulla.

In a few instances focal bacterial lesions were found in the brain. However these cases had other evidences of sepsis, and the bacterial lesions were considered merely evidences of a septic complication such as in one instance pneumonia and in another pyelonephritis.

Since most of the individuals coming to autopsy were of advanced years, the evidences of arteriosclerotic changes in brain, heart, kidney, etc. were often definite and striking. Fully 65 per cent of cases showed arteriosclerotic thickening of the arterioles. Arteriosclerotic nephrosclerosis was found in perhaps one fourth of all cases and myocardial lesions due to the same process in a somewhat smaller percentage of cases.

Bronchopneumonia was the most frequent terminal complication. Usually it was of the purulent lobular type. However, in some cases the pneumonic process resembled closely acute hemorrhagic influenzal pneumonia with destruction of bronchial epithelium, thickening and hyperemia of bronchial walls and a hemorrhagic alveolar exudate with small areas of necrosis of lung tissue.

About one third of all cases showed an acute change in the kidneys apparently related to the disease itself. This consisted of swelling and intense congestion of blood vessels with petechial hemorrhages in the pelvic mucosa. Intranuclear inclusions were observed in the epithelial cells of the convoluted tubules and of Henle's loops in a number of instances[17].

The differences in the pathology of St. Louis Encephalitis as contrasted with the von Economo type of lethargic encephalitis are as follows:

1. The meninges show more intense infiltration with mononuclear cells than is usually found in the lethargic type.

2. Inflammatory foci are more widespread throughout the brain, often occurring in great numbers in the cerebral cortex, and are not restricted to the mid brain and basal ganglia.

3. Degenerative changes in the nerve cells are more frequent and neuronophagia is more marked.

4 The nerve cells in the nuclei of the cranial nerves especially the third rarely shows degenerative changes

5 There is more extensive involvement of the spinal cord

These differences are best noted in the early cases of the epidemic with intense inflammatory reaction Later cases individually might be difficult to differentiate on a pathological basis

Incubation Period

At least eight individuals are known to have developed encephalitis from 4 to 14 days after leaving the St Louis area and showing an incubation of at least 4 and as high as 14 days Six cases developed encephalitis between 9 and 21 days after entering the area involved by the epidemic showing incubation periods no longer than 9 to 21 days[17]

Clinical Course

The disease most often is of sudden onset However, in a considerable percentage of cases malaise headache, dizziness and myalgia preceded the acute onset by a period of several days Symptoms of coryza were described during this period in only some 14 per cent of all cases Actual sore throat was equally rare as an initial symptom Occasionally gastrointestinal symptoms such as nausea and diarrhea preceded the onset of encephalitic symptoms

Sometimes chills but more often chilly feelings occurred at the onset in about one-fourth of all cases The fever as a rule rose rapidly after its onset to attain levels within 48 hours around 105 F in the average case Its subsequent course was quite irregular The duration of febrile period varied between 3 and 37 days with an average duration of 12 days after the onset Eight cases out of 128 had a fever lasting longer than 21 days The fever curve was quite irregular showing in some instances two or even three waves of fever of several days duration dropping almost to normal between The final decline usually was by lysis rather than by crisis Extreme hyperpyrexia was seen often in severe fatal cases The isolation period of three weeks required by the health authorities usually permitted fairly complete recovery before discharge from the hospital

Therefore in contrast to the winter von Economo type of encephalitis we are dealing here with a definite febrile illness Furthermore the nervous symptoms presently to be described are usually more severe in those cases with the highest temperature and cases with low fever usually have few nervous manifestations With the return of temperature to normal levels most cases quickly recovered from the nervous symptoms associated with the disease

Headache was one of the most common symptoms being nearly universally present Often located in the front and top of the head it was described as dull constant often stupefying pain" Accompanying the headache general aching of muscles was noted frequently, sometimes most markedly in the muscles of the back and neck

Definite somnolence was present in approximately two thirds of all cases It deepened to coma in about one fourth of all cases Mental confusion and irrationality occurred in about 40 per cent of cases often with active delirium

In contrast to the von Economo type of lethargic encephalitis cranial nerve palsies were rare Diplopia occurred in less than 10 per cent of cases and as a rule was transitory Unequal or irregular pupils and sluggish or absent light reflexes were observed occasionally Nystagmus was present in about 10 per cent of cases Ptosis was comparatively rare A few cases noted difficulty in swallowing Motor aphasia was noted occasionally

Neck rigidity usually was present during the acute stages of the disease A positive Kernig s sign was noted in about one fourth of all cases There was observed in nearly one third of all cases a generalized spasticity of the muscles This sometimes was merely a feeling of resistance to passive movement but in other instances a marked spasticity occurred Muscular tremors of various distribution and severity also were seen often particularly tongue tremor which was quite common

Nausea and vomiting were of frequent occurrence but seldom persisted very long These appeared at times to be associated with increased spinal fluid pressure Abdominal and cremasteric reflexes in many cases were diminished or absent Tendon reflexes varied in activity sometimes being exaggerated sometimes diminished sometimes unequal Pathological toe signs (Babinski s sign) usually were present at some time during the disease but varied in type and location from day to day and even from hour to hour Ankle clonus was present rarely

Evidences of involvement of organs other than the nervous system occasionally appear The most important was the development of

4 The nerve cells in the nuclei of the cranial nerves, especially the third, rarely shows degenerative changes

5 There is more extensive involvement of the spinal cord

These differences are best noted in the early cases of the epidemic with intense inflammatory reaction Later cases individually might be difficult to differentiate on a pathological basis

Incubation Period

At least eight individuals are known to have developed encephalitis from 4 to 14 days after leaving the St Louis area and showing an incubation of at least 4 and as high as 14 days Six cases developed encephalitis between 9 and 21 days after entering the area involved by the epidemic showing incubation periods no longer than 9 to 21 days[17]

Clinical Course

The disease most often is of sudden onset However in a considerable percentage of cases malaise headache, dizziness and myalgia preceded the acute onset by a period of several days Symptoms of coryza were described during this period in only some 14 per cent of all cases Actual sore throat was equally rare as an initial symptom Occasionally gastrointestinal symptoms such as nausea and diarrhea preceded the onset of encephalitic symptoms

Sometimes chills, but more often chilly feelings occurred at the onset in about one-fourth of all cases The fever as a rule rose rapidly after its onset to attain levels within 48 hours around 103 F in the average case Its subsequent course was quite irregular The duration of febrile period varied between 3 and 37 days with an average duration of 12 days after the onset Eight cases out of 128 had a fever lasting longer than 21 days The fever curve was quite irregular showing in some instances two or even three waves of fever of several days duration dropping almost to normal between The final decline usually was by lysis rather than by crisis Extreme hyperpyrexia was seen often in severe fatal cases The isolation period of three weeks required by the health authorities usually permitted fairly complete recovery before discharge from the hospital

change suggesting the tabetic type of curve in most instances During the febrile stage the average curve found was as follows 111.321000 During the early stages of convalescence after subsidence of the fever the average colloidal gold curve was 1112 1000 Colloidal gold reactions performed several months and even several years after the acute phase while usually found normal in some instances showed a persisting alteration one of the most persistent of the clinical laboratory fingings

Thus case #33-11081 seen in St Louis during the acute phase of the disease in September of 1933 more than 14 months later had a colloidal gold curve showing 12233 111 Several other cases had lesser degrees of reactions after an equally long period

The Virus Neutralization Test

The fact that the convalescent serum of cases of St Louis encephalitis contained neutralizing antibodies against the virus which causes the disease was shown by Webster and Fite[3] The value of this test in the differential diagnosis of the disease was demonstrated by Broun and Rushmin[89] *It is of value in eliminating other virus infections of the nervous system* as well as eliminating confusing conditions due to other causative agents

The technique of this test is as follows[89] A serum specimen is collected close to the time of onset as well as a convalescent serum secured at least weeks and preferably longer after the onset of the disease *In the test each serum is mixed with equal parts of a suspension of an* emulsion in Locke s solution of the brain of a mouse dying of St Louis encephalitis Various dilutions of mouse brain usually 1/10 000 to 1/1 000 000 ordinarily are used The serum virus mixtures then are incubated for 2 hours at 37 C White mice then are inoculated intracerebrally *with the serum virus mixture in the* quantity of 0 0 5 c c 3 to 6 mice being used for each dilution Controls of equal quantities of virus suspensions and normal human serum and a known positive protecting serum and virus mixture should be run simultaneously

Those serum virus mixtures which permit at least 50 per cent survival of the inoculated mice while controls in the same dilution of virus and normal serum fail to give this protection are considered to contain neutralizing antibodies

In a considerable percentage of cases both in the St Louis epidemic of 1933 and that of 1937 negative virus neutralization tests were found in cases which clinically appeared to be typical cases of St Louis

pneumonia This occurred as a terminal event in a number of fatal cases A relatively slow pulse in relation to the height of the fever was noted sometimes in the early part of the febrile period, often to be followed by rather marked tachycardia, which at times persisted into convalescence[98]

Pre-existing pathological conditions, particularly arteriosclerotic and hypertensive vascular disease, were present often to complicate the clinical picture In a series of 130 cases, treated at Firmin Desloge Hospital[18], it was noted that cases with pre-existing hypertension showed a distinctly high mortality from the encephalitis infection Several deaths which occurred from 1 month to 4 years after the acute illness, showed evidence of advanced cerebral vascular disease

Laboratory Findings

Urinary findings except in those cases with pre-existing complications usually were normal Moderate albuminuria together with a few red corpuscles and leucocytes were seen occasionally In several instances cystitis and pyelitis with accompanying pyuria developed as complications

The leucocyte count varied in different cases between leucopenia as low as 5 000 to a leucocytosis as high as 20,000 On the average a slight polymorphonuclear leucocytosis occurred The Schilling differential count showed in most instances a moderate shift to the left However, in few infections of equal febrile reaction is a definite shift to the left in the differential count so often missing There was no tendency for anemia to develop either during the acute phase or during convalescence

The blood non protein nitrogen was normal except in cases of marked dehydration or with preceding renal complications Blood sugar usually was normal but tended to show slightly higher than average figures

The spinal fluid nearly always was clear rarely slightly turbid or bloody The pressure often was somewhat increased Globulin frequently was increased to a moderate extent Spinal fluid sugar in most instances was normal occasionally slightly elevated There seemed no particular tendency to false positive Wassermann or Kahn tests either in spinal fluid or blood

The colloidal gold reaction in the spinal fluid showed a moderate

to be as good or better than before the attack of encephalitis The most common residual noted is a tendency to frequent headaches Nervousness in the sense of excitability and irritability is quite frequent In only a few instances do these reach proportions which seriously disturb family relationships Forgetfulness is another common complaint Difficulty in walking particularly a tendency to deviate to one or the other side occasionally is noted A tendency to persistent mild somnolence or to insomnia occurs fairly frequently but seldom is of severe grade Several cases complained of failing vision and impaired hearing but the fact that many of these patients are of advanced years renders such symptoms difficult of interpretation

A number of patients have died in the intervening years Apoplexy was by far the most frequent cause of death in these cases This suggests the possibility that the vascular lesions of encephalitis may still further weaken the walls of atherosclerotic vessels

Differential Diagnosis

While we have evidence from our clinical experience that some sporadic cases of St Louis encephalitis undoubtedly occur the great majority of the cases that have been observed have been limited to the definite epidemics The occurrence during the late summer and early autumn at a time when mosquitoes are unusually prevalent of a considerable number of cases with fever headache somnolence and signs of meningeal irritation should suggest the possibility that an epidemic of this disease is occurring Poliomyelitis and the equine types of encephalomyelitis however also must be considered

The seasonal incidence the tendency for many individuals of advanced age to be attacked the high fever and relatively brief course with few serious residuals serve to differentiate this infection from lethargic (winter) encephalitis of the von Economo type

The differentiation from lymphocytic choriomeningitis is more difficult Both may have a prodromal illness Both have high fever and signs of meningeal irritation St Louis encephalitis is much more likely to occur in epidemics of considerable size lymphocytic meningitis chiefly as sporadic cases St Louis encephalitis attacks those of advanced years much more frequently In lymphocytic meningitis the spinal fluid cell count in most instances is above 500 cells per cu mm St Louis encephalitis shows cell counts usually below 300 cells per cu mm Isolation of

encephalitis Thus Muckenfuss and associates[100] found 22 per cent with negative tests in cases from the 1933 epidemic In our experience with cases from the 1933 epidemic and also from the 1937 outbreak we found about 20 per cent of the convalescent sera gave negative results These cases must either fail to develop neutralizing antibodies, or they may represent cases of other neurotropic virus diseases with similar clinical manifestations There is already evidence in the literature that lymphocytic choriomeningitis[9] and western equine encephalomyelitis[61 241] may occur simultaneously with cases of St Louis encephalitis It is also noteworthy that the 1937 outbreak of encephalitis in St Louis was accompanied by an increased incidence of poliomyelitis Some obscure cases occurring during encephalitis epidemics may represent cerebral forms of poliomyelitis The neutralization tests with these and other neurotropic viruses which now are available, will have to be carried out in each case to determine the true diagnosis

The use of the complement fixation test in the diagnosis of encephalitis and rabies was described by Casals and Palacios[45] in 1941 This test has been used with successful results in the clinical diagnosis and epidemiological study of Japanese encephalitis by Sabin[144] It is applicable to the study of St Louis encephalitis In a group of 50 apparently normal medical students, residents of the state of Missouri whose sera were collected in 1949 and tested by the complement fixation reaction against St Louis encephalitis virus in the author's laboratory, four showed a positive reaction although in low titre (1/4 to 1/16) This suggests continued exposure to this virus in the St Louis area

Residuals of St Louis Encephalitis

One of the most striking differences between St Louis Encephalitis and the von Economo type of winter encephalitis lies in the paucity of serious nervous residuals in the case of St Louis encephalitis The findings of a recheck of cases, made one year after the epidemic of 1933 has been described by Bredeck, Broun Hempelmann McFadden and Spector[10] Fifteen years of subsequent experience with the 1933 cases has not materially altered the picture as reported after one year Parkinsonism, so common as a chronic residual of winter encephalitis is conspicuous by its absence The great majority of cases have been able to resume their previous occupations Fully two thirds report their health

A series consistently handled along these conservative lines presents a distinctly low mortality[3]

Some efforts at reducing intracranial pressure may perhaps be indicated in cases showing high cerebrospinal fluid pressures Repeated lumbar puncture for this purpose has been advocated by some clinicians Hypertonic glucose or sucrose solutions also found considerable use In stuporous cases the routine emptying of the bladder by catheter often was indicated as a tendency to urinary bladder distention was observed not infrequently Feeding by nasal catheter often was necessary during periods of unconsciousness or where paralysis of the muscles of swallowing was noted

Convalescent serum or transfused blood has been used occasionally No large series of cases is available for accurate evaluation However as in other virus diseases it is questionable whether serum can be effective after the virus has actually invaded the nerve cells and exists as an intracellular parasite In my experience with St Louis encephalitis virus convalescent serum will not protect mice if the inoculation with virus preceeds the administration of the serum Nevertheless Olitsky and Saenz[128] have reported that enormous doses of hyperimmune serum will show some curative effect in western equine encephalomyelitis even though given subsequent to the virus inoculation So perhaps the last word regarding the use of serum has not been said

Animal experiments with chemotherapeutic agents such as sulfanilimide sulfathiazole and sulfadiazine as well as penecillin and streptomycin so far have offered no promise that these substances will be of value in the treatment of St Louis encephalitis An interesting observation is that of Sullivan Zarafonetis and Goth[143] on the beneficial effect of ether anesthesia in animals inoculated with various neurotropic viruses including that of St Louis encephalitis This deserves further study

Webster[90] showed that subcutaneous inoculation of mice with living St Louis encephalitis virus for a time protects the brain from infection The development and widespread use of a vaccine against Japanese B encephalitis without serious harmful effects[144] indicates that development of a similar vaccine for use in epidemics of St Louis encephalitis probably would be entirely practicable However the irregular nature of the outbreaks in any one area and the likelihood that measures for mosquito control would be likely to be effective in future outbreaks make any widespread use of this type of vaccine at this time unnecessary

the virus from the spinal fluid should be attempted and sometimes is possible in lymphocytic meningitis In convalescence virus neutralization tests are of value in the differentiation of these infections

Eastern equine encephalomyelitis frequently runs a brief course to a fatal termination The course of St Louis encephalitis, even in fatal cases is likely to be more prolonged Granular leucocytes usually are quite numerous in the spinal fluid of eastern equine encephalomyelitis rare in the spinal fluid in St Louis encephalitis Convulsions are common in eastern equine encephalomyelitis much less common in St Louis encephalitis The reports so far available regarding cases that have survived eastern equine encephalomyelitis indicate that serious nervous residuals occur they have been rare in St Louis encephalitis History of exposure to sick horses would suggest the possibility of the equine infection, although present evidence would suggest that the intervention of the mosquito is necessary in both diseases History of contact with horses is rare in our experience in St Louis encephalitis

The western variety of equine encephalomyelitis appears to resemble St Louis encephalitis very closely in its clinical manifestations Again the history of exposure to sick horses and mosquitoes should suggest the equine infection The spinal fluid findings may not help greatly in the distinction although the reported average count of 300 cells per cu mm is distinctly higher than that of St Louis encephalitis It is reported that children show a considerable number of granulocytes in the spinal fluid in the equine infection, these are rare in the St Louis type of infection Probably the virus neutralization or the complement fixation test will be the most reliable method of distinction between these two infections This however does not become positive until some time after the onset of the illness

Cerebral forms of poliomyelitis also may present a problem in differential diagnosis Children are the ones most likely to be infected with poliomyelitis Nevertheless St Louis encephalitis does occur in all age groups Virus neutralization tests also may be required for the distinction Muscular palsies are of course rare in St Louis encephalitis and their occurrance should suggest the possibility of poliomyelitis

Treatment

The treatment of this disease consists of careful nursing with particular attention to nutrition during the stage of somnolence and stupor

eastern and western strains of equine encephalomyelitis virus had been the Appalachian mountains Recently a spread of the eastern type to Texas has been reported[140]

Another development in this field has been the isolation of a type of equine encephalomyelitis virus in Venezuela which now is known to attack man[140]

In Bergey's manual[19] this group of viruses is classified as belonging to the genus *Erro* Apparently the three types causing human infection have not been separated but are given the general designation *Erro equinus* The virus causing Borna disease in horses which again is serologically different is designated *Erro bornensis*

Eastern Equine Encephalomyelitis

Definition—An acute infectious disease caused by a filterable virus characterized by acute onset of fever headache delirium and coma It terminates fatally in most cases after a brief course of 3 to 6 days Cases which survive the acute attack may have serious nervous residuals Proven human cases so far have been limited to the New England states although the virus has been isolated from horses as far to the southwest as Texas[140]

Incidence Etiology and Epidemiology

The disease more commonly attacks children than adults although McAdams and Porter[13] have reported an adult case The seasonal incidence is identical with that of other late summer types of encephalitis occurring chiefly in the months of August and September *Preceeding illness such as whooping cough apparently was a predisposing* factor in several cases

Besides the occurrence of this disease in horses it has been shown also to occur spontaneously in wild birds and hence these may act as an additional reservoir of infection In the laboratory the disease has been transmitted successfully by mosquitoes[1, 3, 133] Definitely infected mosquitoes have not yet been found in areas in which human cases developed Hence the mode of transmission while presumably from infected horses and birds by mosquitoes to man is not fully established

In the white mouse which is quite susceptible to infection with

EQUINE ENCEPHALOMYELITIS

Introduction

For many years epidemics of encephalitis have been observed among horses both in Europe and the United States The name of Borna disease has been given to one type of this infection and this is presumably limited to horses Two other virus types of encephalitis which cause infection in horses in the United States, are now known to infect man These are known as eastern and western equine encephalomyelitis The virus causing the infection in the western part of the United States was isolated by Meyer Haring and Howitt[1] in 1931 The same authors reported two cases of encephalitis in men who had been in contact with infected horses in California In 1934 Howitt recovered the same virus from the spinal fluid of a man dying from encephalitis in the same state and later (1938) isolated the virus from brain tissue of a child dying of this disease[124]

Eklund and Blumstein[125] reported 6 cases of human infection occurring in Minnesota in the summer of 1937 Autopsy in one case showed the presence of encephalitis Serum from one case was found to have neutralizing antibodies against the western equine encephalomyelitis virus when examined by Ten Broeck

Kelser[126] in 193--1933 found that the virus of the western type of encephalomyelitis could be transmitted by the *Aedes Aegypti* Subsequently the same author and also Simmons Reynolds and Cornell have found several other types of the aedes mosquitoes can act as carriers More recently Hammon and Reeves[127] find that *Culex tarsalis* is an important carrier of this infection

Merril Lacaillade and Ten Broeck[128] were the first to isolate the eastern strain of equine encephalomyelitis virus from horses They also have shown that it is possible for this infection to be spread by mosquitoes

In the summer of 1938 a definite outbreak of encephalitis occurred both in horses and human beings in Massachusetts[129] This was soon shown to be due to the virus of the eastern variety of equine encephalomyelitis[130, 131]

Therefore it is now known that both the western and the eastern strains of the viruses of encephalomyelitis of horses are pathogenic for man Up to 1942 the geographical dividing line of the distribution of the

Spinal fluid examination shows an increased pressure and a high cell count varying as a rule between 00 and 1 500 per cu mm One feature in which this infection differs from most of the other virus infections of the nervous system is the presence in some cases of large numbers of polymorphonuclear leucocytes as well as lymphocytes in the spinal fluid However Breslich Rowe and Lehman[11] have observed high percentages of granulocytes in the spinal fluid of children infected with western equine encephalomyelitis

Spinal fluid chlorides usually are normal and the sugar content is not decreased Some increase in protein may occur Alteration of the colloidal gold curve usually is present although irregular in type In the monkey the spinal fluid contains the virus suggesting the possibility of its isolation from this source in man

The cases which survive the acute attack usually have shown evidences of extensive damage to the nervous system

Differential Diagnosis

The history of exposure to mosquitoes and horses or the occurrence of the eastern type of the disease among horses in the same vicinity suggest the diagnosis in many cases The sudden violent onset and brief usually fatal course characterized frequently by convulsions are valuable diagnostic criteria The relatively high percentage of granulocytes among the leucocytes of the spinal fluid while bacteria can not be demonstrated is an additional finding which should aid in the differential diagnosis Finally the isolation of the virus by intracerebral inoculations of mice with spinal fluid or brain material secured at autopsy should be attempted In the convalescent stage a rise in complement fixing and virus neutralizing antibodies against this virus in the patient s serum is of great diagnostic value

Treatment and Prevention

No known specific therapy is as yet available The report of Sulkin Zarafonetis and Goth[12] to the effect that ether anesthesia modifies the course and outcome of western equine encephalomyelitis in mice may offer a possible approach to effective treatment The development of an effective vaccine such as that used by Beard Beard and Finklestein[13]

this virus, the disease is of brief duration Adequate doses of virus usually cause death within 48 hours According to Webster[131] monkeys, guinea pigs and sheep are quite susceptible also The rabbit is somewhat less susceptible

Pathology

The pathology of eastern equine encephalomyelitis has been described by McAdams and Porter[13] The meninges show no gross exudate There is marked engorgement of superficial vessels The convolutions are flattened and the sulci narrowed The cut surface shows marked congestion particularly of the white matter The vessels of the cerebrum may be more engorged than those of the pons, medulla and cerebellum

Microscopically there is seen a marked degree of neuronophagia throughout the cerebrum There is also a diffuse infiltration of the cerebral tissues with polymorphonuclear leucocytes, monocytes and microglia Some edema and foci of early ischemic necrosis are present also The blood vessels are seen to be distended with erythrocytes Many contain thrombi some of which are fibrinous and some hyaline Around the vessels are collars of monocytes and polymorphonuclear leucocytes The same type of reaction is present to some extent in the pia arachnoid

The predominance of polymorphonuclear leucocytes among the infiltrating cells is a point of difference between this disease and St Louis encephalitis

Clinical Course

A typical case develops fever and headache neck rigidity delirium and coma Apparently convulsions occur with much greater frequency than in other types of encephalitis The chief additional feature of the clinical picture is its rapid progression to a fatal termination Death occurs much earlier than in other forms of encephalitis occurring usually in 4 to 5 days The immediate mortality is quite high having been around 60 per cent in the Massachusetts outbreak

epidemics usually have occurred mixed with St Louis encephalitis and in circumstances which suggest the importance of mosquitoes as the transmitting agent of this infection This has been brought out largely through the articles of Hammon and his coworkers[10, 22, 23] in their studies of conditions affecting the spread of this disease in the Yakima valley of Washington and elsewhere

They have been able to isolate the western equine virus from mosquitoes *Culex tarsalis* and other species much more frequently than the St Louis encephalitis virus Horses are known to be infected in the areas in which the disease appears and may serve as the source from which human beings are infected Sulkin[11] has reported the isolation of western equine encephalomyelitis virus from chicken mites suggesting that chickens may serve as a reservoir of this infection Hammon was unable to isolate this virus from mites[11] Hence the method of carry over from season to season remains somewhat uncertain

Age and Sex Incidence

The age incidence of this disease appears to be fairly evenly spread among the age groups In California and Minnesota most cases occurred in male adults particularly farmers who had close contact with horses In North Dakota the cases were divided evenly between the two sexes and some cases occurred among professional workers The occurrence of a case in a nurse who had taken care of cases of encephalitis suggests the possibility of transfer of infection from one human being to another In general such transfer would appear to be quite rare

Pathology

Eklund and Blumstein[1] report the pathological findings in a case of western equine encephalomyelitis In this case there was but minimal involvement of the brain tissues and the most marked lesions were in the cervical cord Breslich Rowe and Lehman[1] in a more extensive study of the pathology of this condition found much more involvement of the brain They found definite hyperemia of the leptomeninges with flattening of the convolutions of the cerebrum and narrowing of the sulci The brain tissue on cut section was pink Histologically the leptomeninges were infiltrated diffusely with lymphocytes mixed with

may be of value in prevention in any future epidemics Mosquito control and isolation of known human and equine cases under conditions in which they are protected from contact with mosquitoes should prevent the spread of the disease in times of epidemic, although the reservoir among wild birds may be difficult to control So far the total number of proven human cases of this type of infection is small This is fortunate since the mortality is high and the after effects in surviving cases quite serious

Western Equine Encephalomyelitis

Definition — An acute infectious disease caused by a virus and spread by mosquitoes The virus occurs commonly among horses in the western part of the United States Clinically the disease is characterized by an acute onset with fever headache somnolence, neck rigidity and muscular tremors followed in some instances by delirium and coma The average case terminates in from 2 to 3 weeks The mortality is about [illegible]0 per cent or close to that seen in St Louis encephalitis and distinctly lower than that of eastern equine encephalomyelitis

Historical Account

The disease has been known to occur in California since 1931[135] and has been found in man as far east as Minnesota[1] A rather large outbreak occurred in the late summer of 1938 in North Dakota[101] One of the largest epidemics of encephalitis so far recorded in the United States took place in the late summer and autumn of 1941 It was a mixed epidemic of western equine encephalomyelitis and St Louis encephalitis The states of Minnesota North Dakota South Dakota Montana and Nebraska were most severely involved but surrounding states were affected also to some extent[13, 136, 13, 138, 139]

Etiology and Epidemiology

The earlier reported cases of human infection with the virus of western equine encephalomyelitis occurred in individuals who had had close contact with infected horses The more widespread recent

usually between 10 and 230 mm of water The cell count averages 130 cells per cu mm but counts have varied from 2 to [illegible] The cells in adults are about 80 per cent lymphocytes In children the percentage of granulocytes is higher and may reach 50 per cent

The cases reported from California have been fatal cases mostly but in the North Dakota outbreak the *mortality was approximately* [illegible] *per cent Cases which recovered showed no immediate serious nervous sequels*

Differential Diagnosis

Because of the marked similarity of the clinical picture to that of St Louis encephalitis and because there is evidence that both infections may occur in the same area the differential diagnosis between these two conditions is very difficult The virus neutralization and complement fixation tests probably constitute the most valuable method of differentiation It may be well to recall in this connection that Meyer was unable to secure positive virus neutralization tests in what he believed to be a clinical case We have no information on the percentage of cases that may fail to develop neutralizing antibodies in the blood Isolation of the virus from the brain at autopsy has been accomplished by Howitt So far it has not been isolated from human spinal fluid

The differential diagnosis from lymphocytic choriomeningitis may be difficult also Lymphocytic choriomeningitis usually is preceded by a well defined prodromal illness western equine encephalomyelitis begins suddenly The spinal fluid cell count usually is higher in lymphocytic choriomeningitis Virus neutralization and complement fixation tests also will aid in this differentiation

The seasonal incidence the definite febrile course of relatively brief duration the rarity of ocular palsies and early recovery without marked nervous residuals will serve as a *differentiation from the winter lethargic type of encephalitis*

The presence *of a severe epidemic of encephalomyelitis among horses of a particular area should warn the local medical practitioners that* human *cases of the same infection may occur*

Prevention and Treatment

The control of animal epidemics of western equine encephalomyelitis the isolation of known animal cases mosquito control and isolation

a few plasma cells and epithelioid cells Occasionally a few thrombi and hemorrhages were seen Marked perivascular round cell infiltration occurred in all parts of the brain, less markedly in the cortex than in the basal ganglia pons and medulla The cells were mostly lymphocytes with an occasional plasma cell, epithelioid cell or polymorphonuclear leucocyte Small aggregations of mononuclear cells, probably of glial origin occurred scattered through the brain Degenerative changes in the nerve cells of the basal ganglia pons and medulla were seen also Nuclei appeared more deeply stained but indistinct in outline In some instances the nucleus appeared to have disintegrated or completely dis appeared Foci of demyelination formed a striking feature of the pathological picture These foci were found in basal ganglia, pons and medulla but not in the cerebral cortex The brain tissue was replaced by a palely staining spongy, fibrillar mass These lesions were numerous in some cases rare in others Marked lesions of the olfactory bulbs occurred in two cases raising the question whether a nasal portal of entry might not have been the method of infection in these cases

Clinical Course

As in the case of other forms of summer encephalitis the months of August and September are the periods of greatest prevalence The clinical picture of western equine encephalomyelitis may closely re semble St Louis encephalitis[101] There is usually a sudden onset of fever headache, neck rigidity and mental confusion, sometimes followed by delirium and coma Generalized aching of muscles is common Nausea and vomiting are of frequent occurrance In children convulsions are prone to occur In those cases in which drowsiness deepens to coma the mortality is high

Muscular tremors of face and extremities are seen in attempted move ment but usually are absent in repose Rigidity of the neck and absent abdominal reflexes are the most common physical findings Pathological toe signs such as Babinsky s sign occasionally occur The fever rises rapidly to levels between 101 and 105 F its average duration is 8 days Chills or chilly sensations may occur with high fever Death may occur as early as 4 days after onset

The leucocyte counts of the blood may vary from 5 000 to 2- 000 with an average count of about 12 000 The spinal fluid pressure is

usually between 10 and 230 mm of water The cell count averages 130 cells per cu mm but counts have varied from 2 to 5 5 The cells in adults are about 80 per cent lymphocytes In children the percentage of granulocytes is higher and may reach 50 per cent

The cases reported from California have been fatal cases mostly but in the North Dakota outbreak the mortality was approximately [illegible] per cent Cases which recovered showed no immediate serious nervous sequels

Differential Diagnosis

Because of the marked similarity of the clinical picture to that of St Louis encephalitis and because there is evidence that both infections may occur in the same area[illegible] the differential diagnosis between these two conditions is very difficult The virus neutralization and complement fixation tests probably constitute the most valuable method of differentiation It may be well to recall in this connection that Meyer[illegible] was unable to secure positive virus neutralization tests in what he believed to be a clinical case We have no information on the percentage of cases that may fail to develop neutralizing antibodies in the blood Isolation of the virus from the brain at autopsy has been accomplished by Howitt[illegible] So far it has not been isolated from human spinal fluid

The differential diagnosis from lymphocytic choriomeningitis may be difficult also Lymphocytic choriomeningitis usually is preceded by a well defined prodromal illness western equine encephalomyelitis begins suddenly The spinal fluid cell count usually is higher in lymphocytic choriomeningitis Virus neutralization and complement fixation tests also will aid in this differentiation

The seasonal incidence the definite febrile course of relatively brief duration the rarity of ocular palsies and early recovery without marked nervous residuals will serve as a differentiation from the winter lethargic type of encephalitis

The presence of a severe epidemic of encephalomyelitis among horses of a particular area should warn the local medical practitioners that human cases of the same infection may occur

Prevention and Treatment

The control of animal epidemics of western equine encephalomyelitis the isolation of known animal cases mosquito control and isolation

of known cases offer a promising field for preventive medicine Vaccination of horses against the virus has been tried extensively

Beard, Beard and Finklestein[14] have developed and used a vaccine containing both eastern and western equine encephalomyelitis virus In human beings it caused no severe reactions and resulted in the appearance of virus neutralizing antibodies in the sera of vaccinated individuals They used formolized chick embryo material as a source of virus vaccine

No specific therapy has been developed Treatment is, therefore symptomatic and probably should follow the general lines indicated in the section on St Louis encephalitis Sulkin, Zarafonetis and Goth[13] have reported modification of the course and outcome of experimental infections of mice with western equine encephalomyelitis virus by ether anesthesia This may develop into a possible method of treatment but is still purely in the experimental stage Hyperimmune serum is of some slight benefit early in experimental infections in animals [9]

Venezuelan Equine Encephalomyelitis

Another type of equine encephalomyelitis has been found to be present in several parts of the South American continent[11] It has been demonstrated in Venezuela, Colombia Ecuador and the island of Trinidad The virus has been isolated from animal as well as human sources and its serological characteristics studied The disease is believed to be transmitted by mosquitoes and affects men and horses and perhaps other large mammals

JAPANESE TYPE B ENCEPHALITIS

Definition—An acute infectious disease caused by a filterable virus and occurring in Japan and neighboring areas in the late summer and autumn months and exhibiting in most outbreaks a higher incidence and mortality with advancing age Clinically it is characterized by sudden onset with fever headache somnolence nuchal rigidity and muscular tremors by moderate leucocytosis in the peripheral blood and pleocytosis in the spinal fluid with lymphocytes predominating in that fluid The febrile period usually is of 7 to 14 days duration, and convalescence is slow Permanent nervous residuals are rare

Historical Account

There is evidence in the Japanese medical literature that a form of summer encephalitis has occurred in those islands for many years The disease was first carefully investigated during and after a severe epidemic which took place in 19 4 Kaneko and Aoki[1] who studied the disease at this time are responsible for the distinction of this form of encephalitis from the winter encephalitis described by von Economo[5] They suggested that winter encephalitis should be called type A and summer encephalitis type B

After the epidemic of 1924 summer encephalitis has been recognized as present in Japan in endemic form each year and other epidemic outbreaks have occurred in 19 9 1935 and 1937[18] Studies made by American physicians[141] since the occupation of Okinawa Japan and Korea in 1945 indicate the continued presence of this disease in the native population and some cases have developed in the American forces of occupation

Geographical Distribution

Type B encephalitis has been observed to occur in all of the main Japanese islands with the exception of Hokkaido It has been reported in the Riu Kiu Islands[11] in Formosa[16] Korea Siberia and possibly in China[116 147] The greatest incidence has been in Japan between 30 and 40 N latitude chiefly in districts bordering on the Inland Sea[16]

Climatic Conditions

Outbreaks of Japanese B encephalitis are sharply limited to the late summer and early fall months of August September and October and end with the onset of cool weather About 60 per cent of the cases occur in August and 30 per cent in September the remaining 10 per cent are found to occur mostly in October with occasional late cases in November and early cases in July Epidemic years are likely to be marked by intense heat and scanty rainfall The Tokyo epidemic of 1935 however continued through a period of cool weather[16]

of known cases offer a promising field for preventive medicine Vaccination of horses against the virus has been tried extensively

Beard Beard and Finklestein[14] have developed and used a vaccine containing both eastern and western equine encephalomyelitis virus In human beings it caused no severe reactions and resulted in the appearance of virus neutralizing antibodies in the sera of vaccinated individuals They used formolized chick embryo material as a source of virus vaccine

No specific therapy has been developed Treatment is therefore symptomatic and probably should follow the general lines indicated in the section on St Louis encephalitis Sullivan, Zarafonetis and Goth[149] have reported modification of the course and outcome of experimental infections of mice with western equine encephalomyelitis virus by ether anesthesia This may develop into a possible method of treatment but is still purely in the experimental stage Hyperimmune serum is of some slight benefit early in experimental infections in animals[39]

Venezuelan Equine Encephalomyelitis

Another type of equine encephalomyelitis has been found to be present in several parts of the South American continent[141] It has been demonstrated in Venezuela, Colombia Ecuador and the island of Trinidad The virus has been isolated from animal as well as human sources and its serological characteristics studied The disease is believed to be transmitted by mosquitoes and affects men and horses and perhaps other large mammals

JAPANESE TYPE B ENCEPHALITIS

Definition—An acute infectious disease caused by a filterable virus and occurring in Japan and neighboring areas in the late summer and autumn months and exhibiting in most outbreaks a higher incidence and mortality with advancing age Clinically it is characterized by sudden onset with fever headache somnolence nuccal rigidity and muscular tremors by moderate leucocytosis in the peripheral blood and pleocytosis in the spinal fluid with lymphocytes predominating in that fluid The febrile period usually is of 7 to 14 days duration, and convalescence is slow Permanent nervous residuals are rare

paralysis of extremities as a first sign of disease carry virus in the blood stream during the early stages of infection and are relatively susceptible to intraperitoneal and subcutaneous injections Monkeys given an intra cerebral injection of a small quantity of virus develop an acute fatal encephalitis characterized by cerebellar incoordination and specific necrosis of Purkinje cells Sheep injected intracerebrally or intranasally develop an acute fatal encephalitis but appear to be resistant to sub cutaneous injection Kasahara[11] also studied the immunological characteristics of this virus and regarded it as similar to but not identical with St Louis encephalitis virus

This virus is now recognized as belonging to the genus *Erro* and has been named *Erro japonicus*[19]

The biochemical biophysical and immunogenic properties of Japanese B encephalitis virus have been the subject of investigations carried out by Duffy and Stanley[1] They were unable to separate the virus from other components of a mouse brain suspension by differential centrifugation A considerable portion of the virus was lost or destroyed in the centrifugation process With this procedure they were able to prepare vaccines of about twice the immunogenic potency of the starting material but they did not consider this to be a practical method for the preparation of vaccine The optimal pH range for the activity of this virus appears to be near pH 8 5 Ringer s solution phosphate buffer at pH 7 0 and saline phosphate buffer at pH 8 were poor media for the storage of the virus Most satisfactory as storage media were 10 per cent rabbit serum in saline or phosphate buffer 10 per cent skimmed milk in saline or phosphate buffer and 1 per cent arginine at pH 8 3 Undiluted rabbit serum or undiluted skimmed milk were unsatisfactory as storage media

Mitamura[13] and Inada[14] and other Japanese and Russian investigators have reported that Japanese B encephalitis virus can be transmitted by mosquitoes of two genera namely *Aedes* and *Culex* Reeves and Hammon[15] confirmed the ability of *Aedes* and *Culex* mosquitoes to act as vectors and also incriminated mosquitoes of the genus *Culiseta* They demonstrated transmission by a total of seven species belonging to these three genera Since the work of Reeves and Hammon was done with North American species of mosquitoes it indicated that if introduced into the United States danger of transmission of this virus to the population exists in all areas in which these species of mosquitoes are prevalent

Age and Sex Incidence

Most of the statistics of the age distribution of Japanese B encephalitis show a marked increase in incidence with advancing age[15] In the Tokyo epidemic of 1935 and in cases reported from Formosa and Okinawa there has been reported, on the contrary a high incidence of cases among children Some believe that the disease is so mild, when it attacks children that case reporting is much less complete than in adults[16]

Males are infected somewhat more frequently than females

Case Incidence and Mortality

Although a rather large number of cases have been reported from Japan over a period of years the case incidence per 100 000 population has been 20 5 between the years 1924 and 1933 and the death rate 13 3 per 100 000 population[16] The mortality has varied in epidemic years from 42 to 65 per cent In the Tokyo epidemic of 1935 in which many young people were infected the mortality was lower, being 33 7 per cent

Etiology and Epidemiology

In 1934 the virus of Japanese B encephalitis was successfully transmitted to monkeys by Hayashi[148] In the following year the virus was transmitted to mice by Kasahara, Ueda Okamoto, Yoshida Hamano and Yamada[149] The pathogenicity of this virus for various laboratory animals was studied by Webster[1] particularly in comparison with the St Louis encephalitis virus He concludes that the St Louis virus is pathogenic apparently only for mice and *Macacus rhesus* monkeys Mice injected with this virus usually show as a first sign of disease tremors and convulsions fail to show virus regularly in the blood stream and are resistant to intraperitoneal and subcutaneous injection of all save maximum doses Monkeys injected intracerebrally with massive doses are relatively resistant less than 50 per cent showing a mild non fatal encephalitis Japanese virus on the other hand is pathogenic for mice *Macacus rhesus* monkeys and sheep Mice injected with the virus show

and disorientation commonly are present and a maniacal state may develop This may be followed by deep coma Photophobia nystagmus and diplopia may be noted and various disturbances of speech occur Anuria and constipation are observed frequently as well as urinary and rectal incontinence

The physical signs commonly seen are rigidity of the muscles of the neck and upper extremities The Kernig sign is positive only occasionally Pupillary reactions to light may be sluggish or absent The abdominal reflexes tend to be diminished or absent Children affected by the disease frequently have convulsions Paralysis of the muscles of the extremities often occurs either as a monoplegia or hemiplegia and may be of flaccid or spastic type Transient facial palsy may be noted Bulbar palsy is a frequent cause of death Pneumonia is mentioned as a frequent finding at post mortem examination and may contribute to the fatal outcome[16, 144, 158, 159]

Many mild and abortive cases occur particularly in young individuals[16, 144]

Laboratory Findings

The peripheral blood usually shows a moderate polymorphonuclear leucocytosis usually less than 20 000 per cu mm The examination of the spinal fluid as a rule reveals an increase in pressure of 00 to 300 mm The fluid ordinarily is clear with a lymphocytic pleocytosis rarely greater than 100 per cu mm[144] Some polymorphonuclears may be noted in the fluid close to the onset of the disease The virus has been isolated from the spinal fluid by animal inoculation It can be recovered still more readily from brain tissue of fatal cases

Webster[160] and others[144] have shown that the serum of convalescents and also of exposed individuals not acutely ill with the disease contains neutralizing antibodies against the virus A complement fixation test also has been developed and found to be of practical value in diagnosis[144] A rising titre of antibodies against this virus observed during convalescence may be taken as an indication that the preceding infection was Japanese B encephalitis

Nervous Residuals

After effects from Japanese B encephalitis infection are relatively uncommon Neurasthenia and personality changes[144] are mentioned as

Pathology

The pathology of Japanese B encephalitis has been described by Uchiyama[1] and Hashimoto[1] The chief features are clouding of the meninges by serous exudate with some areas of hemorrhagic exudation seen occasionally In some cases considerable numbers of polymorphonuclear cells were present in the meningeal exudate, in others no polynuclears were present Round cell infiltration was always present

Areas of focal necrosis were found often, some of microscopic size others easily evident to gross inspection These lesions were widespread in distribution, the anterior commissure, red nucleus, substantia nigra quadrigeminal body the cortex, the nuclei of the pons and medulla and the grey matter of the anterior horns of the cord being common locations of the necrotic foci Some of these were abscess-like areas with polymorphonuclear cells others dense masses of round cells, others diffuse areas which might contain round cells, polymorphonuclears rod like cells and changes in the nerve cells

Perivascular infiltrations, mostly composed of lymphocytic cells but with a few polymorphonuclears mononuclears and plasma cells were a marked feature of most cases They were located in the cortex, the walls of the ventricles and the white matter of the hemispheres and cord

Sclerosis and calcification of vessels were seen even in young individuals Fresh hemorrhages usually small in extent were seen in the cortex, white matter and near the anterior commissure Various types of nerve cell degeneration were noted

Pneumonia and bronchitis appeared to be present to some extent in all cases coming to autopsy No significant changes were noted in other organs

Clinical Course

The incubation period of Japanese B encephalitis has not been definitely established There is frequently an afebrile prodromal period of several days duration marked by restlessness, insomnia headache and general malaise[14, 18, 19] This is followed by an abrupt onset of fever severe headache, vomiting, somnolence, delirium and coma Hiccough occasionally is present The maximum temperature usually is between 100 F and 104° F The elevation of temperature persists for several days and as a rule falls by lysis about the 5th or 6th day Delirium

and disorientation commonly are present and a maniacal state may develop This may be followed by deep coma Photophobia nystagmus *and diplopia may be noted and various disturbances of speech occur* Anuria and constipation are observed frequently as well as urinary and rectal incontinence

The physical signs commonly seen are rigidity of the muscles of the neck and upper extremities The Kernig sign is positive only occasionally Pupillary reactions to light may be sluggish or absent The abdominal reflexes tend to be diminished or absent Children affected by the disease frequently have convulsions Paralysis of the muscles of the extremities often occurs either as a monoplegia or hemiplegia and may be of flaccid or spastic type Transient facial palsy may be noted Bulbar palsy is a frequent cause of death Pneumonia is mentioned as a frequent finding at post mortem examination and may contribute to the fatal outcome[16, 144, 158, 159]

Many mild and abortive cases occur particularly in young individuals[16, 144]

Laboratory Findings

The peripheral blood usually shows a moderate polymorphonuclear leucocytosis usually less than 20 000 per cu mm The examination of the spinal fluid as a rule reveals an increase in pressure of 200 to 300 mm The fluid ordinarily is clear with a lymphocytic pleocytosis rarely greater than 100 per cu mm[144] Some polymorphonuclears may be noted in the fluid close to the onset of the disease The virus has been isolated from the spinal fluid by animal inoculation It can be recovered still more readily from brain tissue of fatal cases

Webster[160] and others[144] have shown that the serum of convalescents and also of exposed individuals not acutely ill with the disease contains neutralizing antibodies against the virus A complement fixation test also has been developed and found to be of practical value in diagnosis[144] A rising titre of antibodies against this virus observed during convalescence may be taken as an indication that the preceding infection was Japanese B encephalitis

Nervous Residuals

After effects from Japanese B encephalitis infection are relatively uncommon Neurasthenia and personality changes[144] are mentioned as

having been observed Some persisting paralysis of extremities is noted in some cases Parkinsonism appears to occur very rarely

Treatment

No specific treatment has been developed for Japanese B encephalitis Therapy is therefore, symptomatic, once the disease has developed

Since the disease appears to be spread by mosquitoes epidemics should be controlled by measures designed to eliminate these insects and to protect human beings from contact with them Patients ill with the disease should be protected from contact with mosquitoes to prevent possible ingestion of the virus by these vectors A vaccine prepared from infected mouse brains has been prepared and used by the U S armed forces Its effectiveness is not fully known at this time[14] The preparation and properties of this vaccine have been described by Duffy and Stanley[15]

AUSTRALIAN X-DISEASE

An acute infectious disease with the clinical characteristics of an encephalitis[13, 14] occurred in Australia in 1917 and 1918 and possible recurrences were noted in 19..[16] and 19 5[17] The outbreaks took place during hot weather so that this disease may be classified as one of the summer types of encephalitis It has been given the designation, Australian X-Disease and so far as is known has not spread outside of the geographical limits of that island continent

While occurring at all ages up to 68 years it attacks particularly young children under 5 years of age It is productive of a high mortality, close to 70 per cent Death occurs in many cases after an illness of but a few days duration

A virus was isolated during the early outbreaks by inoculation of human brain material into monkeys Besides for the *Macacus rhesus* monkey the virus was shown to be pathogenic for sheep and also caused illness in a calf and a colt This virus subsequently has been lost so that its serological relationship to other neurotropic viruses is not known In Bergey s manual[19] it has been classified as a member of the encephalitis virus family of *Erronaceae* and given the name *Erro incognitus*

Perdrau[17] felt that the pathological lesions produced by the virus of Australian X disease closely resembled those caused by the virus of louping ill but felt that no claim could be made that they are one and the same virus Some demyelinization was noted in sections of human brain material infected by this virus Louping ill apparently has not been noted in sheep in Australia[4]

Clinically the disease is characterized by high fever mental confusion coma muscular rigidity and convulsions Serious nervous residuals including Parkinsonism were observed in surviving cases

WEST NILE ENCEPHALITIS

In 1940 Smithburn and his coworkers[11] reported isolation of a neurotropic virus from the blood stream of a 37 year old woman a native of Uganda Africa Little is known of the clinical manifestations of this form of encephalitis but antibodies against the virus were found in the blood of other natives in the vicinity The virus is pathogenic for mice and rhesus monkeys but not pathogenic for African monkeys guinea pigs and hedgehogs It has been classified[12] in the genus '*Erro*' and is named *Erro nili*

The virus is of interest in that while it is a distinct virus type it has some serological relationship to the St Louis and Japanese B encephalitis viruses[18]

having been observed Some persisting paralysis of extremities is noted in some cases Parkinsonism appears to occur very rarely

TREATMENT

No specific treatment has been developed for Japanese B encephalitis Therapy is therefore symptomatic once the disease has developed

Since the disease appears to be spread by mosquitoes epidemics should be controlled by measures designed to eliminate these insects and to protect human beings from contact with them Patients ill with the disease should be protected from contact with mosquitoes to prevent possible ingestion of the virus by these vectors A vaccine prepared from infected mouse brains has been prepared and used by the U S armed forces Its effectiveness is not fully known at this time[14] The preparation and properties of this vaccine have been described by Duffy and Stanley[15]

AUSTRALIAN X DISEASE

An acute infectious disease with the clinical characteristics of an encephalitis[13, 14] occurred in Australia in 1917 and 1918 and possible recurrences were noted in 19--[16] and 19 5[17] The outbreaks took place during hot weather so that this disease may be classified as one of the summer types of encephalitis It has been given the designation Australian X-Disease and so far as is known has not spread outside of the geographical limits of that island continent

While occurring at all ages up to 68 years it attacks particularly young children under 5 years of age It is productive of a high mortality close to 70 per cent Death occurs in many cases after an illness of but a few days duration

A virus was isolated during the early outbreaks by inoculation of human brain material into monkeys Besides for the *Macacus rhesus* monkey the virus was shown to be pathogenic for sheep and also caused illness in a calf and a colt This virus subsequently has been lost so that its serological relationship to other neurotropic viruses is not known In Bergey s manual[19] it has been classified as a member of the encephalitis virus family of *Erronaceae* and given the name *Erro incognitus*

Perdrau[37] felt that the pathological lesions produced by the virus of Australian X disease closely resembled those caused by the virus of louping ill but felt that no claim could be made that they are one and the same virus. Some demyelinization was noted in sections of human brain material infected by this virus. Louping ill apparently has not been noted in sheep in Australia[174]

Clinically the disease is characterized by high fever, mental confusion, coma, muscular rigidity and convulsions. Serious nervous residuals including Parkinsonism were observed in surviving cases.

WEST NILE ENCEPHALITIS

In 1940 Smithburn and his coworkers[11] reported isolation of a neurotropic virus from the blood stream of a 37 year old woman, a native of Uganda, Africa. Little is known of the clinical manifestations of this form of encephalitis, but antibodies against the virus were found in the blood of other natives in the vicinity. The virus is pathogenic for mice and rhesus monkeys but not pathogenic for African monkeys, guinea pigs and hedgehogs. It has been classified[19] in the genus *Erro* and is named *Erro nili*.

The virus is of interest in that, while it is a distinct virus type, it has some serological relationship to the St. Louis and Japanese B encephalitis viruses[14]

GROUP IV

Encephalitis and Virus Meningitis With Irregular Seasonal Distribution

LYMPHOCYTIC CHORIOMENINGITIS

Synonyms—Aseptic meningitis benign lymphocytic meningitis

Definition—An acute infectious disease caused by a filterable virus The onset sometimes is sudden but often is preceded by a prodromal illness suggesting mild influenza or a gastrointestinal infection High fever, severe headache mental confusion and other evidences of meningeal irritation develop The spinal fluid shows a markedly elevated count of lymphocytic cells without the presence of bacteria

Introduction and Historical Account

Wallgren[19] in 1925 described the clinical picture of lymphocytic meningitis The criteria which he laid down for its diagnosis are quoted by Baird and Rivers[104] as follows sudden onset of meningeal symptoms associated with slight or moderate increase in the number of cells especially lymphocytes in a bacteria free spinal fluid, a benign course with no complications the absence of foci of acute or chronic infection in the vicinity of the brain for example sinusitis and the absence from the community of diseases known to be capable of producing irritation of the meninges

These criteria offer little that would differentiate this condition from St Louis encephalitis western equine encephalomyelitis or any form of encephalitis, where meningeal symptoms are prominent The requirement that diseases known to be capable of producing irritation of the meninges must be absent from the community would exclude its recognition whenever any type of encephalitis is present

Many clinicians following these criteria have described many cases of aseptic meningitis or lymphocytic meningitis" Baird and Rivers[104] have shown that many of these cases give no serological evidence of being true cases of lymphocytic meningitis although the clinical findings in some instances may be indistinguishable Their exact classification remains uncertain

In the following account the clinical picture as presented is based

on cases in the author's own experience and those found in the literature in which either the virus was actually isolated or in which positive virus neutralization tests gave suggestive evidence that the cases were true cases of lymphocytic choriomeningitis

The definite differentiation of lymphocytic choriomeningitis from other forms of infection of the central nervous system was established through the work of Armstrong and Lillie [illegible] These investigators reported in 1934 that they had encountered a previously unidentified virus in the fifth transplant in monkeys of brain material originally secured from an individual who died in St Louis during the encephalitis epidemic of 1933 They expressed some doubt whether the virus had been secured from the original brain material or had occurred spontaneously in one of the monkeys used in the inoculations Later these same authors isolated this virus from human brain materials proving its occurrence as an infection in man

Rivers and Scott[105] *reported in detail two clinical cases in which they* succeeded in isolating the virus from the spinal fluid The virus has been isolated also from the spinal fluid by Findlay Alcock and Stern[106] in England and Broun Muether and Greutter have isolated the virus from *the spinal fluid of a non fatal case in St Louis and have serological* evidence of the occurrence of another case as early as 193 Traub[107] in Princeton N J and Lepine and associates[108] in France have found this virus as the causative agent of spontaneous infection in white mice

Armstrong, Wooley and Onstott[109] *have studied the virus neutraliza*tion tests in serum collected from various parts of the United States Their results indicate that some 11 per cent of the population of the country show positive protective power in their serum against this virus *Since the number having a history of an acute illness with nervous symp*toms is far less than this they believe that there are many abortive cases and that many other cases occur also in which the manifestations of the virus invasion are noted in areas other than the central nervous system *Their studies in the monkey indicate that the virus is not strictly neu*rotropic but can attack many organs and tissues[110] They found that children show fewer positive reactions than do adults

Geographical Distribution

There is evidence at the present time that this virus occurs in *France*[108], *England*[106] *Ireland*[111] *and the United States In the United*

GROUP IV

Encephalitis and Virus Meningitis With Irregular Seasonal Distribution

LYMPHOCYTIC CHORIOMENINGITIS

Synonyms—Aseptic meningitis benign lymphocytic meningitis

Definition—An acute infectious disease caused by a filterable virus The onset sometimes is sudden but often is preceded by a prodromal illness suggesting mild influenza or a gastrointestinal infection High fever severe headache mental confusion and other evidences of meningeal irritation develop The spinal fluid shows a markedly elevated count of lymphocytic cells without the presence of bacteria

Introduction and Historical Account

Wallgren[19] *in 1925 described the clinical picture of lymphocytic* meningitis The criteria which he laid down for its diagnosis are quoted by Baird and Rivers[101] as follows 'sudden onset of meningeal symptoms associated with slight or moderate increase in the number of cells especially lymphocytes in a bacteria free spinal fluid, a benign course with no complications, the absence of foci of acute or chronic infection in the vicinity of the brain for example, sinusitis and the absence from the community of diseases known to be capable of producing irritation of the meninges'

These criteria offer little that would differentiate this condition from St Louis encephalitis, western equine encephalomyelitis or any form of encephalitis where meningeal symptoms are prominent The requirement that diseases known to be capable of producing irritation of the meninges must be absent from the community, would exclude its recognition whenever any type of encephalitis is present

Many clinicians following these criteria have described many cases of aseptic meningitis or lymphocytic meningitis" Baird and Rivers[101] have shown that many of these cases give no serological evidence of being true cases of lymphocytic meningitis, although the clinical findings in some instances may be indistinguishable Their exact classification remains uncertain

In the following account the clinical picture as presented is based

on cases in the author's own experience and those found in the literature in which either the virus was actually isolated or in which positive virus neutralization tests give suggestive evidence that the cases were true cases of lymphocytic choriomeningitis

The definite differentiation of lymphocytic choriomeningitis from other forms of infection of the central nervous system was established through the work of Armstrong and Lillie[9] These investigators reported in 1934 that they had encountered a previously unidentified virus in the fifth transplant in monkeys of brain material originally secured from an individual who died in St Louis during the encephalitis epidemic of 1933 They expressed some doubt whether the virus had been secured from the original brain material or had occurred spontaneously in one of the monkeys used in the inoculations Later these same authors isolated this virus from human brain materials proving its occurrence as an infection in man

Rivers and Scott[3] reported in detail two clinical cases in which they succeeded in isolating the virus from the spinal fluid The virus has been isolated also from the spinal fluid by Findlay Alcock and Stern[116] in England and Brown Muether and Greutter have isolated the virus from the spinal fluid of *a non fatal* case in St Louis and have serological evidence of the occurrence of another case as early as 193 Traub[10] in Princeton N J and Lepine and associates[105] in France have found this virus as the causative agent of spontaneous infection in white mice

Armstrong Wooley and Onstott[109] *have studied the virus neutraliza*tion tests in serum collected from various parts of the United States Their results indicate that some 11 per cent of the population of the country show positive protective power in their serum against this virus Since the number *having a history of an acute illness with nervous symp*toms is far less than this they believe that there are many abortive cases and that many other cases occur also in which the manifestations of the virus invasion are noted in areas other than the central nervous system *Their studies in the monkey* indicate that the virus is not strictly neurotropic but can attack many organs and tissues[110] They found that children show fewer positive reactions than do adults

Geographical Distribution

There is evidence at the present time that this virus occurs in *France*[108], *England*[106] *Ireland*[111] *and the United States*[9] *In the United*

States most of the proven cases have been along the Atlantic seaboard or in the Mississippi valley There is good reason to believe from the studies of Armstrong Wooley and Onstott[103] that the infection is wide spread

Etiology and Epidemiology

The virus etiology of lymphocytic choriomeningitis has been established by the work described in the previous sections In Bergey s manual [19] the virus has been classified as belonging to the same genus, *Legio* as the virus of poliomyelitis and has been named *Legio erebea* The virus is not strictly neurotropic and can be introduced into the body by various routes Armstrong and Wooley found the virus infectious by urethral and vaginal instillation suggesting the possibility of a venereal mode of transmission The virus has been found as a spontaneous infection in man monkeys and mice It has been experimentally transmitted to the guinea pig hamster rat, dog, ferret and the chick embryo

The observations of Armstrong and Sweet[114] and of Armstrong, Wallace and Ross[11] point to the gray mouse *Mus musculus* as a reservoir of the disease from which it spreads to man These observers have demonstrated the presence of the virus in gray mice trapped in the homes of 4 patients with proved lymphocytic choriomeningitis, residents of Washington D C and of one patient in Lancaster Pa The probability of mice being the source of human infection has been enhanced by the study[116] of a patient at the Peter Bent Brigham Hospital, Boston, Mass with proved lymphocytic choriomeningitis This patient had handled a male mouse especially its genetalia 3 days before developing a sensation of feeling tired followed in ten days more by fever, malaise and drowsiness In the home of this individual subsequently mice were trapped and the virus of lymphocytic choriomeningitis demonstrated to be present in these animals Dalldorf Jungeblut and Umphler[138] recently have reported multiple human cases in an apartment house harboring infected mice in Raleigh N C The virus was isolated both from human beings and mice living in this apartment The human cases were spread over a period of several years

Armstrong and his associates[114] proved that 64 mice from 34 different homes in Washington D C were infected of a total of 122 examined (52 per cent) 41 of 6[illegible] mice (66 per cent) from [illegible]2 homes harboring

infected mice when tested were found to be immune to the virus. In Washington 1 out of every [illegible] mice examined was found to be a carrier of the virus. The observations indicate extensive infection of mice with the virus of lymphocytic choriomeningitis.

Traub[11] has shown that an infected mother mouse may convey the infection to her offspring and that such congenitally infected mice may carry the infection for months. Haas[11] has confirmed at the National Institute of Health in Washington the findings of Traub and has shown that mice congenitally infected are much more effective transmitters of the infection to other mice than are those artificially inoculated.

These observations point to mice as probable sources of lymphocytic choriomeningitis infection in man. Armstrong has suggested that transfer to man may occur by way of the gastrointestinal tract[115] or respiratory tract[119]. He believes that the virus escapes from infected mice by way of the urine and nasal secretions. The patient at the Peter Bent Brigham Hospital[116] suggests that possibly finger transmission may occur from virus in the mouse's feces or urine, presumably finger to mouth in man. If so, then mice can easily infect food with the virus and by such food man can become infected.

These possibilities, even probabilities, remain, however, as possibilities since direct proof is lacking. Laboratory infection of workers inoculating and studying virus-infected mice is[illegible] further suggestive evidence of the role of mice in the spread of lymphocytic choriomeningitis in man. Lepine, Mollaret and Kreis[illegible] have produced the disease in man by subcutaneous inoculations with mouse virus. Evidence of contact infection in man is lacking except for that in the Peter Bent Brigham Hospital patient as described in preceding sections.

Pathology

The pathology of lymphocytic choriomeningitis has been studied carefully in the monkey by Lillie[110]. In this animal are found almost constantly irregular, more or less pronounced lymphocytic infiltrations of the choroid plexus of the cerebral ventricles, sometimes accompanied by serocellular exudation into the ventricles. Likewise there is an almost constant but moderate, irregularly distributed lymphocytic infiltration of the leptomeninges. Very few foci of cellular gliosis and of vessel sheath infiltration occur in the brain and cord substance in contrast with the picture seen in encephalitis. Meningeal and plexus infiltration may

persist for long periods after infection Focal lymphocyte infiltration and sheath cell proliferation occur in the spinal root ganglia

The lungs often present congestion, serous exudation interstitial edema hemorrhages and perivascular lymphocytic infiltration Pyelitis and sometimes hemorrhagic cystitis occurred in a number of animals and are characterized by focal and diffuse mucosal lymphocytic infiltration and edema Foci of coagulative to fibrinoid hemorrhagic necrosis in the liver are seen in about one fourth of the animals, and focal necroses also occur in the adrenals and parathyroid

Splenic congestion a variable grade of bone marrow hyperplasia and lymph node follicle hyperplasia and sinus reticuloendotheliosis are other frequent findings A focal interstitial, perivascular, lymphocytic infiltration is frequent in kidney epididymis, uterus fallopian tubes parathyroid heart lung intestinal mucosa and occasionally in esophageal mucosa pancreas adrenal testes ovary and skeletal muscles

Very few fatal human cases have been studied In one case described by Haymaker and Smadel in a publication from the Army Medical Museum there was a severe encephalomyelitis of widespread distribution with the brain stem and hippocampus involved most severely Perivascular collars of lymphocytic cells and areas of necrosis in which many glial cells had congregated were prominent features The vessel walls had become hyperplastic In the hippocampus edema and toxic changes in the ganglion cells were noted

Clinical Course

Baird and Rivers[161] have published an extensive study of cases of lymphocytic choriomeningitis comparing cases in which the virus has been isolated or in which positive neutralization tests confirmed the diagnosis with other cases in which the diagnosis was made on clinical findings alone

An interesting feature of the clinical course is the occurrence in about two thirds of the proven cases of an influenza-like prodrome This precedes the acute onset by a week or ten days It is manifested by malaise headache sometimes coryzal symptoms and mild fever After persisting one to three days a distinct remission of one to four days occurs during which the patient feels well enough to resume his occupation This is followed by the acute onset of meningeal symptoms Some

cases on the other hand begin very suddenly and no history of such a prodromal illness is obtainable

The acute phase usually is ushered in with severe headache fever and mental confusion In some instances abdominal pain nausea and vomiting occur at the onset of this disease At least one case complained of burning on urination suggesting the occurrence of urethritis or cystitis

Neck rigidity accompanied in most instances by a positive Kernig s sign soon developed Mental confusion delirium and coma are seen in most cases for varying periods of time Fever rises to levels of 100 to 104 F in most instances but a few afebrile cases have been reported Hyperactive or hypoactive or unequal tendon reflexes are seen frequently but are inconstant Positive toe signs Babinski s sign appear irregularly in most cases These are the most common neurological findings

Findlay Alcock and Stern[100] have reported severe and long persisting muscular palsies in cases observed by them Transient facial palsies muscular weakness and loss of sensation have been recorded also

Most cases recover within about two weeks although cases have been described in which symptoms have persisted for one to two months[100] While the mortality probably is low several fatal cases are included in the few definitely proven cases so far studied A large number of cases of aseptic meningitis have been reported but as Burd and Rivers[101] have shown it is likely that most of these have been caused by some other etiological agent than the virus of lymphocytic choriomeningitis

Laboratory Findings

The urinalysis shows in some cases moderate amounts of albumin sometimes with a slight increase in leucocytes The peripheral blood as a rule reveals a slight polymorphonuclear leucocytosis with a shift to the left in the Schilling differential It should be pointed out that granulocytes predominate in the peripheral blood during the same period in which the spinal fluid shows a high count of lymphocytic cells The blood and spinal fluid Wassermann and Kahn tests are not affected by *this infection in cases so far observed*

The spinal fluid frequently is under increased pressure It may be clear or turbid depending on the cell count A positive globulin test and a sugar content at the lower limits of normal i e between 45 and 55

mgm per 100 c c, usually are found but the marked reduction in sugar content seen in tuberculous and other bacterial forms of meningitis has not been observed here The chloride content of the spinal fluid likewise is at the lower limits of normal The cell count is above 300 per cu mm in the vast majority of cases and above 1,000 per cu mm in about one-half of the known cases The average is therefore, distinctly higher than in most cases of encephalitis The differential count on the spinal fluid shows in most instances between 90 and 100 per cent of lymphocytic cells

The colloidal gold reaction usually shows some alteration from the normal but widely different types of curves have been reported in different cases A curve resembling that of tabes dorsalis is perhaps the most common

The fluid shows no bacteria in smear or culture Inoculation of the fluid intracerebrally into white mice has resulted in the isolation of the virus in a number of instances The animals become sick and die about the seventh to eighth day as a rule Guinea pigs and monkeys also are susceptible Such is the clinical picture and laboratory findings of the typical severe case

There are cases on record where no meningeal symptoms were noted but merely a history of "grippe" and yet following this neutralizing antibodies against the virus of lymphocytic choriomeningitis were found in the patients serum This shows that abortive cases of obscure symptomatology undoubtedly occur The high percentage of sera in the general population which neutralize the virus far outnumbering known cases with meningeal symptoms is further evidence for the existence of these abortive cases

Differential Diagnosis

It is obvious that this infection can be easily confused with tuberculous meningitis and with cases of encephalitis in which meningeal symptoms are prominent

In cases of tuberculous meningitis where tubercle bacilli are found, the differentiation is of course easy Where the bacteria are so few as to escape detection the following differential points are to be kept in mind The spinal fluid in tuberculous meningitis usually shows a distinctly reduced chloride and sugar content It also as a rule shows a considerable admixture of polymorphonuclear leucocytes with the lym

phocytes in cases where the cell count is high Cases with low cell counts however may have a pure lymphocytic picture as does lymphocytic meningitis The outcome of tuberculous meningitis has been practically universally fatal most cases of lymphocytic choriomeningitis recover

The differentiation of lymphocytic choriomeningitis from cases of St Louis encephalitis certainly is extremely difficult It is true that the average age incidence differs in that young adults are attacked most frequently by lymphocytic choriomeningitis and those of advanced years are most susceptible to St Louis encephalitis However both diseases can occur at any age period The seasonal incidence of St Louis encephalitis is limited very largely to the months of August September and October Lymphocytic choriomeningitis seems most common in the autumn and spring months but has been reported in all seasons

The clinical picture and laboratory findings of St Louis encephalitis and lymphocytic choriomeningitis may be highly similar In general however most cases of lymphocytic choriomeningitis show spinal fluid cell counts above 300 per cu mm the vast majority of cases of St Louis encephalitis have cell counts below 300 Here again however there is definite overlapping in exceptional cases

The isolation of the virus from the spinal fluid has been accomplished several times in the case of lymphocytic choriomeningitis It has not been accomplished so far in cases of St Louis encephalitis

Virus neutralization tests and complement fixation tests are the most reliable methods of differential diagnosis provided that specimens of serum are collected at proper intervals to reveal the rise in antibodies during convalescence Smadel Baird and Wall[113] have reported on the use of the complement fixation reaction in lympocytic choriomeningitis

TREATMENT

No specific treatment is available as yet for this infection Cases require careful nursing particularly during periods of delirium and coma Maintenance of adequate nutrition by feeding through nasal catheter may become necessary Intense headache may require relief by use of salicylates codeine or morphine or some of the more recently developed analgesics

Lowering of the pressure of the spinal fluid by puncture and withdrawal of fluid seem at times to relieve headache and to make the patient

more comfortable Hypertonic glucose or sucrose given intravenously may be of value for their effect in lowering spinal fluid pressure

LOUPING ILL

Louping ill is an infection involving the nervous system and caused by a filterable virus which is endemic in sheep in Northern England and Scotland Infection of shepherds by this virus has not been reported but human infection has occurred in laboratory workers in several instances[15] Since these cases had no particular seasonal incidence it appears proper for the time being, to list this infection among those with indefinite seasonal distribution However the close serological relationship between the virus of this disease and that of Russian spring summer tick borne encephalitis must not be forgotten [16] This relationship is particularly close in the cases of encephalitis appearing in European Russia [17]

The virus of louping ill is classified as belonging to the viruses of the genus *Erro* and is termed *Erro scoticus* [13] Besides sheep and man monkeys mice rats horses cattle and pigs have been found to be susceptible to infection by this virus In sheep the transmission from animal to animal probably is by the bite of ticks resembling in this respect Russian encephalitis All proven human cases, however have occurred as accidental laboratory infections

While one case believed to be due to this virus had symptoms resembling an influenzal infection others had definite encephalitic symptoms In these cases a prodromal period of several days duration occurred characterized by fever headache and malaise This was followed by a sudden increase in the severity of these symptoms as well as the appearance of signs of meningeal irritation Diplopia blurring of vision and photophobia various cranial nerve palsies and changes in deep and superficial reflexes occurred

The spinal fluid showed an increased cell count with mononuclear cells predominating There was a slight polymorphonuclear leucocytosis in the peripheral blood

Diagnosis was established by the appearance of virus neutralizing antibodies against the virus of louping ill in the blood serum of these patients during convalescence

All cases eventually recovered without nervous residuals

BIBLIOGRAPHY

Encephalitis Historical

1 ADAMS FRANCIS The Genuine Works of Hippocrates translated from the Greek Wm Wood & Co New York 1849
HECKER J F C The Epidemics of the Middle Ages translated by B G Babington for the Sydenham Society George Woodfall and Son London 1844
3 LATHAM R G The Works of Thomas Sydenham M D translated from the Latin edition of Dr Greenhill printed for the Sydenham Society by C and J Adlard London 1848
4 STERN FELIX Die Epidemische Encephalitis Julius Springer Berlin 19 2
5 von ECONOMO C Encephalitis lethargica Wien klin Woch 1917 XXX 581
6 HEINE JACOB von Beobachtungen uber Lahmungszustander der unteren Extremitat F H Kohler Stuttgart 1840
7 STRUMPELL A Über die akute Enzephalitis der Kinder Jahrb f Kinderheilk 1885 XXII 173
8 LEICHTENSTERN Mittheilungen uber die Influenzaepidemie in Koln Deutsch med Woch 1890 XVI 509
9 EBSTEIN W Bemerkungen uber die sogenannte Nona Klin Woch 1891 XLI 1005
10 OSLER Sir Wm and McCRAE THOS The Principles and Practice of Medicine Eighth Ed New York and London 1916
11 OBREGIA URECHIA and CARNIOL Encephalitis hemorragique avec un diplocoque encapsule Spitalul 1916 No 15 18 347 quoted from Report of Matheson Commission[13]
1 CRUCHET R MONTIER and CALMETTES Quarante cas d encephalomyélite subaigue Bull et Mem Soc med d Hop de Paris 1917 XLI 614
13 CLELAND J B and BRADLEY B Mysterious disease Med Jour Australia 1917 I 499
14 CLELAND J B and CAMPBELL A W Acute encephalomyelitis a clinical and experimental investigation of an Australian epidemic Brit Med Jour 1919 I 663
15 KANEKO R and AOKI Y Ueber die Encephalitis epidemica in Japan Ergebniss d inn Med u Kinderheilk 1928 XXXIV 34
16 THIRD REPORT BY THE MATHESON COMMISSION Epidemic Encephalitis Columbia Univ Press New York 1939
17 REPORT ON THE ST LOUIS OUTBREAK OF ENCEPHALITIS Public Health Bull No 214 1935

18 RIVERS T M and SCHWENTKER F F Louping ill in man Jour Exp Med 1934 LIX, 669
19 WALLGREN A Une nouvelle maladie infectieuse du systeme nerveux central? Acta Pediat 1925, IV 158
o ARMISTRONG C and LILLIE R D Experimental lymphocytic choriomeningitis of monkeys and mice produced by a virus encountered in studies of the 1933 St Louis encephalitis epidemic Pub Health Rep 1934 XLIX 1019
-1 MEYER K F HARING, C M and HOWITT B F Etiology of epizootic encephalomyelitis of horses in the San Joaquin valley 1930 Science 1931 LXXIV 2 7
-2 TEN BROECK C and MERRILL M H A serological difference between eastern and western equine encephalomyelitis virus Proceed Soc Exp Biol and Med 1933 XXXI 217

Lethargic Encephalitis

3 REPORT OF A SURVEY BY THE MATHESON COMMISSION Epidemic Encephalitis Columbia Univ Press New York 19 9
4 ETIENNE G Une epidemie militaire de myelitis aigues Bull Acad de Med 19 7 LXXVII 153
-5 REPORT OF AN ENQUIRY INTO AN OBSCURE DISEASE ENCEPHALITIS LETHARGICA Great Bretain Local Gov Bd n s No 121 1918
6 NETTER A Encephalite lethargique epidemique Bull Acad de Med 1918 LXXIX 337
7 STAHELIN R Ueber Encephalomyelitis epidemica (Encephalitis lethargica) Schweiz med Woch 19-0 I 201
8 MORQUIO L Sobre la encephalitis letargica Rev Med d Uruguay 19 0 XXIII 455
9 NEAL J B Meningeal conditions noted during the epidemic of influenza Jour Am Med Assoc 1919 LXXII 714
30 SECOND REPORT BY THE MATHESON COMMISSION Epidemic Encephalitis Columbia Univ Press New York 193
31 AMOSS H L Immunological distinction of encephalitis and poliomyelitis Jour Exp Med 19 1 XXXIII 187
, STRUMPELL A Ueber Encephalitis epidemica (Encephalitis lethargica) Deutsch med Woch 19 0 XLVI 705
33 FLEXNER S Obvious and obscure infections of the central nervous system Jour Am Med Assoc 19 8 XCI 1

34 FRANCIS T Jr MAGILL T BECK M and RICHARD E Studies with human influenza virus Jour Am Med Assoc 1937 CIX 566
35 HALL, A J Epidemic Encephalitis J Wright & Son Bristol 19 4
36 FLEXNER S Epidemic (lethargic) encephalitis and allied conditions Jour Am Med Assoc 19 3 LXXXI 1688
37 ZINSSER H Present state of knowledge regarding encephalitis Arch Path 19 8 VI 271
38 HARRIS W Acute infectious ophthalmioplegia or botulism Lancet 1918 I 568
39 von WIESNER R R Aetiologie der Encephalitis lethargica Wien klin Woch 1917 XXX 93
40 von ECONOMO C Encephalitis lethargica Wien med Woch 1923 LXXIII 777 835 1113 1 43 and 1334
41 LOEWE, L HIRSHFELD S and STRAUSS I Studies in epidemic encephalitis (encephalitis lethargica) Jour Infect Dis 1919 XXV 378
4 FLEXNER S Virus encephalitis in the rabbit Proceed Nat Acad Sci 19 5 XI 84
43 LEVADITI C and NICOLAU S Encephalites du lapin Compt rend Soc de Biol 1923 LXXXIX 775
44 LEVADITI C SCHOEN R and SANCHIS BAYARRI V Encephalite spontanee du lapin provoquee par le Toxoplasma cuniculi Compt rend Soc de Biol 1927 XCVII 169
45 RIVERS T M and STEWART F W Virus III encephalitis Jour Exp Med 1928 XLVIII 603
46 ROSENOW E C Diaphragmatic spasms in animals produced with a streptococcus from epidemic hiccup Preliminary report Jour Am Med Assoc 19 1 LXXVI 1745
47 ROSENOW E C Experimental studies on the etiology of encephalitis report of findings in one case Jour Am Med Assoc 19 2 LXXIX 443
48 ROSENOW E C Localization in animals of streptococci from cases of epidemic hiccup encephalitis spasmodic torticollis and chorea Arch Neurol and Psychiat 19 8 XIX 4 4
49 McKINLEY E B Failure to confirm Rosenow s work on encephalitis with relation to green streptococcus Proceed Soc Exp Biol and Med 1930 XXVII 436
50 ZINSSER H Present state of knowledge regarding encephalitis Arch Path 1928 VI 271
51 LEVADITI C and HARVIER P Le virus de l encephalite lethargique Compt rend Soc de Biol 19 0 LXXXIII 354

18 RIVERS, T. M. and SCHWENTKER, F. F. Louping ill in man. Jour. Exp. Med. 1934, LIX, 669.

19 WALLGREN, A. Une nouvelle maladie infectieuse du système nerveux central. Acta Pediat. 1925, IV, 158.

20 ARMSTRONG, C. and LILLIE, R. D. Experimental lymphocytic choriomeningitis of monkeys and mice produced by a virus encountered in studies of the 1933 St. Louis encephalitis epidemic. Pub. Health Rep. 1934, XLIX, 1019.

21 MEYER, K. F., HARING, C. M. and HOWITT, B. F. Etiology of epizootic encephalomyelitis of horses in the San Joaquin valley, 1930. Science 1931, LXXIV, 227.

22 TEN BROECK, C. and MERRILL, M. H. A serological difference between eastern and western equine encephalomyelitis virus. Proceed. Soc. Exp. Biol. and Med. 1933, XXXI, 217.

Lethargic Encephalitis

23 REPORT OF A SURVEY BY THE MATHESON COMMISSION. Epidemic Encephalitis. Columbia Univ. Press, New York, 1929.

24 ETIENNE, G. Une épidémie militaire de myélites aigues. Bull. Acad. de Méd. 1917, LXXVII, 153.

25 REPORT OF AN ENQUIRY INTO AN OBSCURE DISEASE, ENCEPHALITIS LETHARGICA. Great Britain Local Gov. Bd. n.s. No. 121, 1918.

26 NETTER, A. Encéphalite léthargique épidémique. Bull. Acad. de Méd. 1918, LXXIX, 337.

27 STAEHELIN, R. Ueber Encephalomyelitis epidemica (Encephalitis lethargica). Schweiz. med. Woch. 1920, I, 101.

28 MORQUIO, L. Sobre la encephalitis letargica. Rev. Med. d. Uruguay 1920, XXIII, 455.

29 NEAL, J. B. Meningeal conditions noted during the epidemic of influenza. Jour. Am. Med. Assoc. 1919, LXXII, 714.

30 SECOND REPORT BY THE MATHESON COMMISSION. Epidemic Encephalitis. Columbia Univ. Press, New York, 1932.

31 AMOSS, H. L. Immunological distinction of encephalitis and poliomyelitis. Jour. Exp. Med. 1921, XXXIII, 187.

32 STRÜMPELL, A. Ueber Encephalitis epidemica (Encephalitis lethargica). Deutsch. med. Woch. 1920, XLVI, 705.

33 FLEXNER, S. Obvious and obscure infections of the central nervous system. Jour. Am. Med. Assoc. 1928, XCI, 21.

34 FRANCIS T Jr MAGILL T BECK M and RICHARD F Studies with human influenza virus Jour Am Med Assoc 193 CIX 566
35 HALL A J Epidemic Encephalitis J Wright & Son Bristol 19 4
36 FLEXNER S Epidemic (lethargic) encephalitis and allied conditions Jour Am Med Assoc 19 3 LXXXI 1768
37 ZINSSER H Present state of knowledge regarding encephalitis Arch Path 1928 VI 71
38 HARRIS W Acute infectious ophthalmoplegia or botulism Lancet 1918 I 568
39 von WIESNER R R Aetiologie der Encephalitis lethargica Wien klin Woch 1917 XXX 93
40 von ECONOMO C Encephalitis lethargica Wien med Woch 19 3 LXXIII 777 835 1113 1 43 and 1334
41 LOEWE L HIRSHFELD S and STRAUSS I Studies in epidemic encephalitis (encephalitis lethargica) Jour Infect Dis 1919 XXV 378
4 FLEXNER S Virus encephalitis in the rabbit Proceed Nat Acad Sci 19 5 XI 84
43 LEVADITI C and NICOLAU S Encephalites du lapin Compt rend Soc de Biol 19 3 LXXXIX 771
44 LEVADITI C SCHOEN R and SANCHIS BAYARRI V Encephalite spontanee du lapin provoquee par le Toxoplasma cuniculi Compt rend Soc de Biol 19 XCVII 169
45 RIVERS T M and STEWART F W Virus III encephalitis Jour Exp Med 1928 XLVIII 603
46 ROSENOW E C Diaphragmatic spasms in animals produced with a streptococcus from epidemic hiccup Preliminary report Jour Am Med Assoc 19 1 LXXVI 1745
47 ROSENOW E C Experimental studies on the etiology of encephalitis report of findings in one case Jour Am Med Assoc 192 LXXIX 443
48 ROSENOW E C Localization in animals of streptococci from cases of epidemic hiccup encephalitis spasmodic torticollis and chorea Arch Neurol and Psychiat 19 8 XIX 4 4
49 McKINLEY F B Failure to confirm Rosenow s work on encephalitis with relation to green streptococcus Proceed Soc Exp Biol and Med 1930 XXVII 436
50 ZINSSER H Present state of knowledge regarding encephalitis Arch Path 1928 VI 71
51 LEVADITI C and HARVIER P Le virus de l encephalite lethargique Compt rend Soc de Biol 1920 LXXXIII 354

52 LEVADITI C HARVIER P and NICOLAU S Étude expérimentale de l encephalite dite 'lethargique', Ann de l Inst Pasteur 19 XXXVI 63
53 LEVADITI C and HARVIER P Recherches expérimentales sur l encephalite lethargique Compt rend Soc de Biol 19 o LXXXIII, 674
54 KLING C DAVIDE H and LILJENQUIST F L encephalite épidémique expérimentale chez le lapin I Virus d origine cerebrale II Virus d origine nasopharyngee Compt rend Soc de Biol 19 1 LXXXV 118.
55 LEVADITI C NICOLAU S and SCHOEN R L'etiologie de l encephalite epizotique du lapin dans ses rapports avec l etude expérimentale de l encephalite lethargique Encephalitozoon cuniculi Ann de l Inst Pasteur 19 4 XXXVIII 651
56 KORITSCHONER R Ueber die Ueberimpfung Enzephalitisvirus auf Hunde Wien klin Woch 19 3 XXXVI 385
57 KOBAYASHI R Studies on virus of experimental encephalitis Japan Med World 1925 V 145
58 FLEXNER S Epidemic encephalitis and simple herpes Jour Gen Physiol 19 4 VIII 713
59 COWDRY E V Comparison of the virus obtained by Kobayashi from cases of encephalitis with virus rabies Jour Exp Med 19 7 XLV 799
60 DOERR, R and VÖCHTING K Études sur le virus de l herpes febrile Rev gen d Ophthalmol 19 o XXXIV 409
61 BLANC G Recherches expérimentales sur le virus de l herpes Compt rend Acad de Sci 19 1 CLXXII 7 5
62 DOERR R and SCHNABEL A Das Virus des Herpes febrilis und seine Beziehungen zum Virus der Encephalitis epidemica (lethargica) Zeitschr f Hyg u Infektionskrankh 19 1 XCIV 29
63 DOERR R and SCHNABEL A Das Virus des Herpes febrilis und seine Beziehungen zum Virus der Encephalitis epidemica (lethargica), Zeitschr f Hyg u Infektionskrankh 19 1 XCIV 290, Herpes- und Encephalitisvirus Schweiz med Woch 19 LII 3 5
64 LEVADITI C HARVIER P and NICOLAU S Conception etiologique de l encephalite epid mique Compt rend Soc de Biol 19 1, LXXXV, 213
65 PERDRAU J R The virus of encephalitis lethargica Brit Jour Exp Path 19 5 VI 1 3
66 FLEXNER S and AMOSS H L Contribution to the pathology of experimental virus encephalitis I An exotic strain of encephalitogenic virus Jour Exp Med 19 5 XLI 215

67 REYS L I Encephalite Epidemique A Maloine et Fils Paris 19
68 MERRITT, H H and FREMONT-SMITH F The Cerebrospinal Fluid W B Saunders & Co Philadelphia 1938
69 PARSONS A C Post encephalitis and its problems Proceed Roy Soc Med 19 8 XXI 1307
70 MAIN ASHIE Lethargic encephalitis the Glasgow epidemic of 19 3 Its incidence and consequences from the point of view of public health Jour Hygiene 1931 XXXI 16
71 HOWE, H A The prognosis of epidemic encephalitis in children Bull Johns Hopkins Hosp 1930 XLVII 1 3
72 STERN F Die Epidemische Encephalitis . Auflage Julius Springer Berlin 1928 review in Jour Nerv and Ment Dis 1930 LXXI 68
73 von ECONOMO C Die Encephalitis lethargica ihre Nachkrankheiten und ihre Behandlung Berlin 19 9 quoted in Epidemic Encephalitis Second Report of the Matheson Commission New York 193
74 KLEEMANN A Mitteilungen zur Therapie der chronischen Encephalitis Deutsch Zeitschr f Nervenheilk 19 9 CXI 99
75 PANEGROSSI G Sulle recenti acquisizioni nella cura del parkinsismo encefalitico Policlin 19,5 XLII 1487
76 NEAL, J B Bulgarian belladonna treatment of chronic encephaliti New York State Med Jour 1939 XXXIX 1875
77 FAPING H C Bulgarian belladonna treatment of post encephalitic parkinsonian syndrome Ohio State Med Jour 1939 XXXV 1191
78 COOPER H A The mental sequelae of chronic epidemic encephalitis and their prognosis Lancet, 1936 II 6,7
79 PRINZMETAL, M and BLOOMBERG W The use of benzedrine for the treatment of narcolepsy Jour Am Med Assoc 1935 CV 2051
80 DAVIS P and STEWART W Benzedrine sulfate in postencephalitic Parkinsonism Jour Am Med Assoc 19 8 CX 1890
81 MATTHEWS R A Symptomatic treatment of chronic encephalitis with benzedrine sulfate Am Jour Med Sci 1938 CXCV 448

Epidemic Summer Encephalitis, St Louis Type

82 BROWN G O CREUTTER J MUETHER R and CASEY A The virus of the 1937 outbreak of encephalitis in St Louis Weekly Bull St Louis Med Soc 1937 XXXII 40
83 CASEY A E and BROWN G O Epidemiology of St Louis encephalitis Science 1938 LXXXVIII 450

52 LEVADITI C HARVIER P and NICOLAU S Étude expérimentale de l'encéphalite dite léthargique, Ann de l'Inst Pasteur 19 XXXVI 63

53 LEVADITI C and HARVIER P Recherches expérimentales sur l'encéphalite léthargique Compt rend Soc de Biol 19 0 LXXXIII 674

54 KLING C DAVIDE H and LILJENQUIST F L'encéphalite épidémique expérimentale chez le lapin I Virus d'origine cérébrale II Virus d'origine nasopharyngée Compt rend Soc de Biol 19 1 LXXXV 118

55 LEVADITI C NICOLAU S and SCHOEN R L'étiologie de l'encéphalite épizootique du lapin dans ses rapports avec l'étude expérimentale de l'encéphalite léthargique Encephalitozoon cuniculi Ann de l'Inst Pasteur 1924 XXXVIII 651

56 KORITSCHONER Ueber die Ueberimpfung Enzephalitisvirus auf Hunde Wien klin Woch 19 3 XXXVI 385

57 KOBAYASHI R Studies on virus of experimental encephalitis Japan Med World 19 5 V 145

58 FLEXNER S Epidemic encephalitis and simple herpes Jour Gen Physiol 19 4 VIII 713

59 COWDRY E V Comparison of the virus obtained by Kobayashi from cases of encephalitis with virus rabies Jour Exp Med 19 7, XLV 799

60 DOERR R and VÖCHTING K Études sur le virus de l'herpes fébrile Rev gen d'Ophthalmol, 19 0 XXXIV 409

61 BLANC G Recherches expérimentales sur le virus de l'herpes Compt rend Acad de Sci 19 1 CLXXII 7 5

62 DOERR R and SCHNABEL A Das Virus des Herpes febrilis und seine Beziehungen zum Virus der Encephalitis epidemica (lethargica) Zeitschr f Hyg u Infektionskrankh 19 1 XCIV, 29

63 DOERR R and SCHNABEL A Das Virus des Herpes febrilis und seine Beziehungen zum Virus der Encephalitis epidemica (lethargica) Zeitschr f Hyg u Infektionskrankh 19 1 XCIV 90, Herpes- und Encephalitisvirus Schweiz med Woch 19 LII 325

64 LEVADITI C HARVIER P and NICOLAU S Conception étiologique de l'encéphalite épidémique Compt rend Soc de Biol 19 1 LXXXV, 213

65 PERDRAU J R The virus of encephalitis lethargica Brit Jour Exp Path 19 5 VI 1 3

66 FLEXNER S and AMOSS H L Contribution to the pathology of experimental virus encephalitis I An exotic strain of encephalitogenic virus Jour Exp Med 19 5 XLI 215

67 REYS I L Encephalite Epidemique A Maloine et Fils Paris 19
68 MERRITT H H and FREMONT SMITH F The Cerebrospinal Fluid W B Saunders & Co Philadelphia 1938
69 PARSONS A C Post encephalitis and its problems Proceed Roy Soc Med 19 8 XXI 1307
70 MAIN ASHIE Lethargic encephalitis the Glasgow epidemic of 19 3 Its incidence and consequences from the point of view of public health Jour Hygiene 1931 XXXI 16
71 HOWE H A The prognosis of epidemic encephalitis in children Bull Johns Hopkins Hosp 1930 XLVII 1 3
7 STERN F Die Epidemische Encephalitis Auflage Julius Springer Berlin 19 8 review in Jour Nerv and Ment Dis 1930 LXXI 68
73 von ECONOMO C Die Encephalitis lethargica ihre Nachkrank heiten und ihre Behandlung Berlin 19 9 quoted in Epidemic Encephalitis Second Report of the Matheson Commission New York 193
74 KLEEMANN A Mitteilungen zur Therapie der chronischen Encephalitis Deutsch Zeitschr f Nervenheilk 19 9 CXI 99
75 PANEGROSSI G Sulle recenti acquisizioni nella cura del parkinsonismo encefalitico Policlin 1935 XLII 1487
76 NEAL J B Bulgarian belladonna treatment of chronic encephalitis New York State Med Jour 1939 XXXIX 1875
77 FABING H C Bulgarian belladonna treatment of post-encephalitic parkinsonian syndrome Ohio State Med Jour 1939 XXXV 1195
78 COOPER H A The mental sequelae of chronic epidemic encephalitis and their prognosis Lancet 1936 II 677
79 PRINZMETAL M and BLOOMBERG W The use of benzedrine for the treatment of narcolepsy Jour Am Med Assoc 1935 CV 051
80 DAVIS P and STEWART W Benzedrine sulfate in postencephalitic Parkinsonism Jour Am Med Assoc 1938 CX 1890
81 MATTHEWS R A Symptomatic treatment of chronic encephalitis with benzedrine sulfate Am Jour Med Sci 1938 CXCV 448

Epidemic Summer Encephalitis St Louis Type

8 BROWN G O GREUTTER J MUETHER R and CASEY A The virus of the 1937 outbreak of encephalitis in St Louis Weekly Bull St Louis Med Soc 1937 XXXII 40
83 CASEY A E and BROWN G O Epidemiology of St Louis encephalitis Science 1938 LXXXVIII 450

52 LEVADITI C HARVIER P and NICOLAU S Étude experimentale de l encephalite dite lethargique' Ann de l Inst Pasteur 19 XXXVI 63
53 LEVADITI C and HARVIER P Recherches experimentales sur l encephalite lethargique Compt rend Soc de Biol 19 o LXXXIII, 674
54 KLING C DAVIDE H and LILJENQUIST F L encephalite epidemique experimentale chez le lapin I Virus d origine cerebrale II Virus d origine nasopharyngee Compt rend Soc de Biol, 19 1 LXXXV 118
55 LEVADITI C NICOLAU S and SCHOEN R L etiologie de l encephalite epizotique du lapin dans ses rapports avec l etude experimentale de l encephalite lethargique Encephalitozoon cuniculi Ann de l Inst Pasteur 1924 XXXVIII 651
56 KORITSCHONER R Ueber die Ueberimpfung Enzephalitisvirus auf Hunde Wien klin Woch 19 3 XXXVI 385
57 KOBAYASHI R Studies on virus of experimental encephalitis Japan Med World 19 5 V 145
58 FLEXNER S Epidemic encephalitis and simple herpes Jour Gen Physiol 19 4 VIII 713
59 COWDRY E V Comparison of the virus obtained by Kobayashi from cases of encephalitis with virus rabies Jour Exp Med 19 7 XLV 799
60 DOERR R and VÖCHTING K Études sur le virus de l herpes febrile Rev gen d Ophthalmol 1920 XXXIV 409
61 BLANC G Recherches experimentales sur le virus de l herpes Compt rend Acad de Sci 19 1 CLXXII 7 5
62 DOERR R and SCHNABEL A Das Virus des Herpes febrilis und seine Beziehungen zum Virus der Encephalitis epidemica (lethargica), Zeitschr f Hyg u Infektionskrankh 19 1 XCIV 9
63 DOERR R and SCHNABEL A Das Virus des Herpes febrilis und seine Beziehungen zum Virus der Encephalitis epidemica (lethargica) Zeitschr f Hyg u Infektionskrankh 19 1 XCIV 90 Herpes- und Encephalitisvirus Schweiz med Woch 19 - LII 3 5
64 LEVADITI C HARVIER P and NICOLAU S Conception etiologique de l encephalite epidemique Compt rend Soc de Biol 19 1 LXXXV, 213
65 PERDRAU J R The virus of encephalitis lethargica Brit Jour Exp Path 19 5 VI 1 3
66 FLEXNER S and AMOSS H L Contribution to the pathology of experimental virus encephalitis I An exotic strain of encephalitogenic virus Jour Exp Med 1925 XLI -15

67 REYS L I Encéphalite Épidemique A Maloine et Fils Paris 19
68 MERRITT H H and FREMONT SMITH F The Cerebrospinal Fluid W B Saunders & Co Philadelphia 1938
69 PARSONS A C. Post encephalitis and its problems Proceed Roy Soc Med 19 8 XXI 1307
70 MAIN ASHIE Lethargic encephalitis the Glasgow epidemic of 19 3 Its incidence and consequences from the point of view of public health Jour Hygiene 1931 XXXI 16
71 HOWE, H A The prognosis of epidemic encephalitis in children Bull Johns Hopkins Hosp 1930 XLVII 123
7 STERN F Die Epidemische Encephalitis Auflage Julius Springer Berlin 19 8 review in Jour Nerv and Ment Dis 1930 LXXI 68
73 von ECONOMO C. Die Encephalitis lethargica ihre Nachkrankheiten und ihre Behandlung Berlin 19 9 quoted in Epidemic Encephalitis, Second Report of the Matheson Commission New York 197
74 KITTMANN A Mitteilungen zur Therapie der chronischen Encephalitis Deutsch Zeitschr f Nervenheilk 19 9 CXI 299
75 PANECROSSI G Sulle recenti acquisizioni nella cura del parkinsonismo encefalitico Policlin 1935 XLII 1487
76 NEAL J B Bulgarian belladonna treatment of chronic encephalitis New York State Med Jour 1939 XXXIX 1875
77 FABING H C. Bulgarian belladonna treatment of post encephalitic parkinsonian syndrome Ohio State Med Jour 1939 XXXV 1195
78 COOPER H A The mental sequelae of chronic epidemic encephalitis and their prognosis Lancet 1936 II 677
79 PRINZMETAL, M and BLOOMBERG W The use of benzedrine for the treatment of narcolepsy Jour Am Med Assoc 1935 CV 051
80 DAVIS P and STEWART W Benzedrine sulfate in postencephalitic Parkinsonism Jour Am Med Assoc 1938 CX 1890
81 MATTHEWS R A Symptomatic treatment of chronic encephalitis with benzedrine sulfate Am Jour Med Sci 1938 CXCV 448

Epidemic Summer Encephalitis St Louis Type

82 BROUN G O GREUTTER J MUETHER R and CASEY A The virus of the 1937 outbreak of encephalitis in St Louis Weekly Bull St Louis Med Soc 1937 XXXII 40
83 CASEY A E and BROUN G O Epidemiology of St Louis encephalitis Science 1938 LXXXVIII 450

82(92) ENCEPHALITIS AND OTHER VIRUS INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

84 ROSENOW E C Isolation of streptococci in a study of the epidemic of encephalitis in St Louis Proceed Soc Exp Biol and Med 1933 XXXI 285

85 MUCKENFUSS R S ARMSTRONG C and McCORDOCK H A Encephalitis studies on experimental transmission Pub Health Rep 1933 XLVIII 1341

86 WEBSTER L T and FITE G L A virus encountered in the study of material from cases of encephalitis in the St Louis and Kansas City epidemics of 1933 Science 1933 LXXVIII 463

87 BROUN G O MUETHER R O and COLLIER W D Transmission of encephalitis to mice from human brain material preserved 3 months in glycerin and comparison of this virus with the virus of an epidemic of tracheobronchitis and pox present in fowl in the St Louis area simultaneously with the encephalitis epidemic Jour Clin Invest 1934 XIII 701

88 WEBSTER L T and FITE, G L St Louis encephalitis serological relation to Japanese encephalitis and experimental studies on immunity Science 1934 LXXIX 254

89 WEBSTER L T and FITE G L Contribution to the etiology of encephalitis Differentiation of encephalitis by protection tests Proceed Soc Exp Biol and Med, 1933, XXXI, 344

90 WEBSTER, LESLIE T Immunity of mice following subcutaneous vaccination with St Louis encephalitis virus Jour Exp Med 1938 LXVIII 111

91 HODES H L and WEBSTER L T Relation between degree of immunity of mice following vaccination with St Louis encephalitis virus and the titre of the protective antibodies of the serum Jour Exp Med 1938 LXVIII 263

92 HARFORD C G SULKIN S E and BRONFENBRENNER J Infection of mice by feeding of tissues containing the virus of St Louis encephalitis Proceed Soc Exp Biol and Med 1939 XLI 33

93 WEBSTER L T CLOW A D and BAUER J H Experimental studies on encephalitis III Survival of encephalitis (St Louis type) in Anopheles quadrimaculatus Jour Exp Med 1935 LXI 479

94 FULTON J D, GREUTTER J E MUETHER R O HANSS E B and BROUN G O Observations concerning Culex pipiens as a possible carrier of St Louis encephalitis Proceed Soc Exp Biol and Med 1940 XLIV, 255

95 HARFORD C G SULKIN S E and BRONFENBRENNER J Susceptibility of wild mice to the virus of St Louis encephalitis Proceed Soc Exp Biol and Med 1939 XLI 331

96 GREUTTER J F FULTON J D MUETHER R O HANSS F B and BROWN C O Susceptibility of field mice and meadow mice to St Louis encephalitis Proceed Soc Exp Biol and Med 1940 XLIV 253
97 KINSELLA R A and BROWN C O The clinical features of epidemic (St Louis) encephalitis Jour Am Med Assoc 1934 CIII 46
98 BROWN C O Encephalitis visceral manifestations complications and treatment Weekly Bull St Louis Med Soc 1933 XXVIII 8
99 BROWN G O and RUSKIN J Encephalitis the virus neutralization test as an aid in differential diagnosis Jour Missouri State Med Assoc 1936 XXXIII 19
100 MUCKENFUSS R S SMADEL J E and MOORE, E The neutralization of encephalitis virus (St Louis 1933) by serum Jour Clin Invest 1935 XIV 699
101 BRESLICH P J ROWE, P H and LEHMAN W L Epidemic encephalitis in *North Dakota Jour Am Med Assoc* 1939 CXIII 172
102 BREDECK J F BROWN G O HEMPELMANN T C Mc FADDEN J F and SPECTOR H I Follow up studies of the 1933 St Louis epidemic of encephalitis Jour Am Med Assoc 1938 CXI 15
103 JONES A and BOSMLIS G 1937 St Louis epidemic of encephalitis Follow up studies Jour Missouri State Med Assoc 1940 XXXVII 5

Lymphocytic Choriomeningitis

104 BAIRD R D and RIVERS T M Relation of lymphocytic choriomeningitis to acute aseptic meningitis (Wallgren) Am Jour Pub Health 1938 XXVIII 47
105 RIVERS T M and SCOTT T F Meningitis in man caused by a filterable virus I Two cases and method of obtaining a virus from their spinal fluids II Identification of the etiological agent Jour Exp Med 1936 LXIII 397
106 FINDLAY G M ALCOCK N and STERN R The virus etiology of one form of lymphocytic meningitis Lancet 1936 I 650
107 TRAUB E A filterable virus from white mice Jour Immunol 1935 XXIX 69
108 LEPINE, P MOLLARET P and KREIS B Receptivite de l'homme au virus murin de la choriomeningite lymphocytaire Reproduction experimentale de la meningite lymphocytaire benigne Compt rend Acad de Sci 1937 CCIV 1846

109 ARMSTRONG C WOOLLEY J and ONSTOTT R Distribution of lymphocytic choriomeningitis virus in the organs of experimentally inoculated monkeys U S Pub Health Weekly Rep 1936 LI 98

110 LILLIE R D Pathologic histology of lymphocytic choriomeningitis in monkeys U S Pub Health Weekly Rep 1936 LI 303

111 COLLIS W R F Acute benign lymphocytic meningitis Brit Med Jour 1935 II 1148

112 ARMSTRONG C and WOOLLEY J Studies on the origin of a newly discovered virus which causes lymphocytic choriomeningitis in experimental animals U S Pub Health Weekly Rep 1935 L 537

113 SMADEL J E BAIRD R D and WALL M J Complement fixation in infections with virus of lymphocytic choriomeningitis Proceed Soc Exp Biol and Med 1939 XL 71

114 ARMSTRONG C and SWEET L K Lymphocytic choriomeningitis report of two cases with recovery of the virus from gray mice (Mus musculus) trapped in the two infected households Pub Health Rep 1939 LIV 673

115 ARMSTRONG C WALLACE J J and ROSS L Lymphocytic choriomeningitis gray mice Mus musculus a reservoir for the infection Public Health Rep 1940 LV 1222

116 FARMER T W and JANEWAY C A Infections with the virus of lymphocytic choriomeningitis Medicine 1942 XXI 1

117 TRAUB E Factors influencing the persistence of choriomeningitis virus in the blood of mice after clinical recovery Jour Exp Med 1938 LXVIII 229

118 HAAS V Statement on p 1228 of paper by Armstrong Wallace and Ross[115]

119 ARMSTRONG C Studies on choriomeningitis and poliomyelitis Transactions and Studies College of Physicians Philadelphia 1940 VIII 1

120 SCOTT T McN and RIVERS T M Meningitis in man caused by a filterable virus Jour Exp Med 1936 LXIII 397

121 LEPINE P and SAUTTER V Contamination de la laboratoire avec le virus de la choriomeningite lymphocytaire Ann Inst Pasteur Paris 1938 LXI 519

122 UNPUBLISHED CASE at Nat Institute of Health Washington D C 1939 cited by Armstrong Wallace and Ross[115]

123 LEPINE P MOLLARET P and KREIS B Receptivite de l homme au virus murin de la choriomeningite lymphocytaire benigne Compt rend de l Acad d Sci 1937 CCIV 831

Equine Encephalomyelitis

1 4 HOWITT B Recovery of the virus of equine encephalomyelitis from the brain of a child Science 1938 LXXXVIII 455

1 5 LKLUND C M and BLUMSTEIN A The relation of human encephalitis to encephalomyelitis Jour Am Med Assoc, 1938 CXI 1734

1 6 KELSER R A Manual of Veterinary Bacteriology, 3rd Ed Williams and Wilkins Co Baltimore 1938

1 7 SIMMONS J S REYNOLDS F and CORNELL V Transmission of virus of equine encephalomyelitis through Aedes albopticus skuze Am Jour Trop Med 1936 XVI 89

1 8 MERRILL, M H LACAILLADE, C W and TEN BROECK, C Mosquito transmission of equine encephalomyelitis Science 1934 LXXX 51

1 9 WESSELHOEFT C SMITH E and BRANCH C Human encephalitis Eight fatal cases with four due to the virus of equine encephalomyelitis Jour Am Med Assoc 1938 CXI 1735

130 FOTHERGILL L D DINGLE J FARBER S and CONNERLY M Human encephalitis caused by the virus of the eastern variety of equine encephalomyelitis New Eng Jour Med 1938 CCXIX 411

131 WEBSTER L T and WRIGHT F H Recovery of eastern encephalomyelitis virus from brain tissue of human cases of encephalitis in Massachusetts Science 1938 LXXXVIII 305

13 McADAMS J C and PORTER J E Encephalitis in man caused by virus of equine encephalomyelitis Report of case in adult New Eng Jour Med 1939 CCXXI 163

133 SIMMONS J S The United States army s war in the air against mosquito borne diseases Am Jour Med Sci 1938 CXCVI 165

134 MEYER K F A summary of recent studies on equine encephalomyelitis Ann Int Med 193 VI 645

135 LEAKE, J P Epidemic of infectious encephalitis Pub Health Rep 1941 LVI 190

136 WHEELER J A Western equine encephalomyelitis occurring in Kansas in human beings in the summer of 1941 Jour Am Med Assoc 1941, CXVII 1972

137 RICHTER R B Western equine encephalomyelitis occurring in a metropolitan area Jour Am Med Assoc 194 CXIX 486

138 YOUNG G A YOUNG R and COUTSKY J Encephalitis in Nebraska during the summer of 1941 Dis Nerv Syst 1943 IV 4

139 MEIKLEJOHN G and HAMMON, W McD Epidemic of encephalitis predominantly of the St Louis type in Pinal County Arizona Jour Am Med Assoc, 1942, CXVIII 960

140 HAMMON W McD and REEVES, W C Recent advances in epidemiology of arthropod borne virus encephalitis Am Jour Pub Health 1945 XXXV 994

141 SULKIN S E Recovery of equine encephalomyelitis virus (Western type) from chicken mites Science 1945 CI 381

142 BEARD J W BEARD, D and FINKLESTEIN H Vaccination of man against the virus of equine encephalomyelitis (eastern and western strains) Jour Immunol, 1940 XXXVIII 117

143 SULKIN S E ZARAFONETIS C and GOTH A Influence of anaesthesia on experimental neurotropic virus infections, Jour Exp Med 1946 LXXXIV 277

Japanese Type B Encephalitis

144 SABIN A B Epidemic encephalitis in military personnel Jour Am Med Assoc 1947 CXXXIII 281

145 HODES H L THOMAS L and PECK J L Cause of an outbreak of encephalitis established by means of complement fixation tests Proceed Soc Exp Biol and Med 1945 LX 220

146 WARREN J Epidemic encephalitis in the Far East, Am Jour Tropical Med, 1946 XXVI 417

147 KUTTNER A G and T UNG T Encephalitis in North China Jour Clin Invest 1936 XV 525

148 HAYASHI M Übertragung des Virus von Encephalitis epidemica japonica auf Affen Zentralbl f d Ges Neurol u Psychiat, 1937 LXXXVI 564

149 KASAHARA S UEDA M OKAMOTO Y YOSHIDA S HAMANO R and YAMADA R Experimental studies on epidemic encephalitis 1 Transmission test of the Japanese encephalitis in 1935 and some characteristics of the infectious agent, Kitasato Arch Exp Med 1936 XIII 48

150 WEBSTER L T Japanese B encephalitis virus its differentiation from the St Louis virus and relationship to louping ill virus, Science 1937 LXXXVI 40

151 KASAHARA S YAMADA R and HAMANO R Experimental studies on epidemic encephalitis 4 Immunological comparison of the Japanese (B type) and American (St Louis) types Kitasato Arch Exp Med 1937 XIV 2 9

152 DUFFY C E and STANLEY W M Studies on biochemical biophysical and immunogenic properties of Japanese B type encephalitis virus and vaccines Jour Exp Med 1945 LXXXII 385
153 MITAMURA T YAMADA S HAZATO H MORI K HOSOI T KITAOKA M WANATABE S OKUBO K and TENJIN S Über den Infectionmodus der Epidemischen enzephalitis Experimentelle Untersuchungen uber ihre Austrekung durch Mucken Trans Japan Path Soc 1937 XXVII 573 quoted in the Third Report of the Matheson Commission see reference 16
154 INADA R Du mode d infection dans l encephalite épidemique Presse méd 1937 XLV 386
155 REEVES W C and HAMMON W McD Laboratory transmission of Japanese B encephalitis virus by seven species (three genera) of North American mosquitoes Jour Exp Med 1946 LXXXIII 185
156 UCHIYAMA T Pathological studies of encephalitis epidemica of 19 4 in Japan Japan Med World 19 5 V 345
157 HASHIMOTO H KUDO M and URAGUCHI K Experiences in the summer epidemic of acute encephalitis in Tokyo Jour Am Med Assoc 1936 CVI 1 66
158 INADA R Observations cliniques sul l encephalite epidemique Gaz de Hop 1938 CXI 11 5
159 KANEKO, R On the epidemic encephalitis which occurred in Japan in 19 4 Japan Med World 1925 V 37
160 WEBSTER L T Japanese B encephalitis virus its differentiation from the St Louis encephalitis and relationship to louping ill Jour Exp Med 1938 LXVII 609

Herpes Simplex Encephalitis

161 NEAL JOSEPHINE B The encephalitis problem Jour Am Med Assoc 1934 CIII 726
162 SMITH M G LENETTE E H and REAMS H R Isolation of the virus of herpes simplex and the demonstration of intranuclear inclusions in a case of acute encephalitis, Amr Jour Path 1941 XVII 55
163 ZARAFONETIS C J SMADEL J F ADAMS J W and HAYMAKER W Fatal herpes simplex encephalitis in man Amer Jour Path, 1944 XX 4 9

139 MEIKLEJOHN G and HAMMON, W McD Epidemic of encephalitis predominantly of the St Louis type in Pinal County Arizona Jour Am Med Assoc, 1942, CXVIII 960
140 HAMMON W McD and REEVES W C Recent advances in epidemiology of arthropod borne virus encephalitis Am Jour Pub Health 1945 XXXV, 994
141 SULKIN S L Recovery of equine encephalomyelitis virus (Western type) from chicken mites Science 1945 CI 381
142 BEARD J W BEARD, D and FINKLESTEIN H Vaccination of man against the virus of equine encephalomyelitis (eastern and western strains) Jour Immunol 1940 XXXVIII 117
143 SULKIN S L ZARAFONETIS, C and GOTH A Influence of anaesthesia on experimental neurotropic virus infections, Jour Exp Med 1946 LXXXIV 277

Japanese Type B Encephalitis

144 SABIN A B Epidemic encephalitis in military personnel Jour Am Med Assoc 1947 CXXXIII 281
145 HODES H L THOMAS L and PECK J L Cause of an outbreak of encephalitis established by means of complement fixation tests Proceed Soc Exp Biol and Med 1945 LX 220
146 WARREN J Epidemic encephalitis in the Far East, Am Jour Tropical Med, 1946 XXVI 417
147 KUTTNER A G and TUNG T Encephalitis in North China Jour Clin Invest., 1936 XV 525
148 HAYASHI M Übertragung des Virus von Encephalitis epidemica japonica auf Affen, Zentralbl f d Ges Neurol u Psychiat, 1937, LXXXVI, 564
149 KASAHARA S UEDA M OKAMOTO Y YOSHIDA S HAMANO R and YAMADA R Experimental studies on epidemic encephalitis 1 Transmission test of the Japanese encephalitis in 1935 and some characteristics of the infectious agent Kitasato Arch Exp Med 1936 XIII 48
150 WEBSTER L T Japanese B encephalitis virus its differentiation from the St Louis virus and relationship to louping ill virus Science 1937 LXXXVI 402
151 KASAHARA S YAMADA R and HAMANO R Experimental studies on epidemic encephalitis 4 Immunological comparison of the Japanese (B type) and American (St Louis) types Kitasato Arch Exp Med 1937 XIV 2 9

Post Influenzal Encephalitis

179 HASSIN G B Acute (hemorrhagic) encephalitis with report of cases Med Record 1909 LXXV 3

180 HURST J H The relationship of influenza and epidemic encephalitis Med Bull Vet Admin 1934 XI 110

181 NEAL J B and WILCOX H L Does the virus of influenza cause neurological manifestations Science 1937 LXXXVI 267

182 BROWN C O MULTHER R O PINKERTON H and LeCIER M Influenzal encephalitis Jour Lab and Clin Med 1945 XXX 39

183 HENLE G and HENLE W Neurologic signs in mice following intracerebral inoculation of influenza viruses Science 1944 C 410

Encephalitis Following Measles and German Measles

184 FORD F R The nervous complications of measles Bull Johns Hopkins Hosp 19 8 XLIII 140

185 MALMUD N Encephalomyelitis complicating measles Arch Neurol and Psychiat 1937 XXXVIII 10 5

186 MERRITT H H and KOSKOFF Y D Encephalomyelitis following German measles Am Jour Med Sci 1936 CXCI 690

187 READ C T Meningo encephalitis and rubella Jour Am Med Assoc 1937 CIX 654

188 DAVISON C and FRIEDFELD L Acute encephalomyelitis following German measles Am Jour Dis Child 1938 LV 496

Encephalitis Following Small Pox

189 ROLLESTON J D Acute infectious diseases nd Edition London 19 9

190 RICE, R M and CAREY M J Hemiplegia due to small pox Jour Am Med Assoc 1933 C, 817

191 FINLEY K H Perivenous changes in acute encephalitis associated with vaccination variola and measles Arch Neurol and Psychiat 1937 XXXVII 305

164 WHITMAN L WAIL M J and WARREN J Herpes simplex encephalitis report of 2 fatal cases Jour Am Med Assoc 1946 CXXI 1408

165 ZINSSER H Herpes encephalitis in monkeys Jour Exp Med 19 9 XLIX 661

Post Infectious Encephalitis General Discussion

166 GREENFIELD J G Acute disseminated encephalomyelitis as a sequel to influenza Jour Path and Bacteriol 1930 XXXIII, 453

167 NEAL J B and APPELBAUM E Encephalitis associated with measles Jour Am Med Assoc 19 7 LXXXVIII 1552

168 BRIGGS J F Meningo encephalitis following rubella Jour Pediat 1935 VII 609

169 LARKIN W R Mumps meningitis found at Camp Taylor Base Hospital with autopsy findings Illinois Med Jour 19 0 XXXVIII 133

170 McINTOSH J and SCARFF R W The history of some virus infections of the central nervous system Proceed Roy Soc Med 19 8 XXI 705

171 COMBY J Encephalite aigue d origine vaccinale Bull et Mem d Hop de Paris 19 6 L 1434

172 ZIMMERMAN H M and YANNETT H Non-suppurative encephalomyelitis accompanying chicken pox Arch Neurol and Psychiat 1931 XXVI 322

173 ELEY R C Neurological conditions in infants and children Jour Pediat 1936 IX 797

174 NEAL JOSEPHINE B Encephalitis Grune and Stratton New York 1942

175 GREENFIELD, J G The pathology of measles encephalomyelitis Brain 19 9 LII 171

176 MARSDEN J P and HURST E W Acute perivascular myelinoclasia (acute disseminated encephalomyelitis) in small pox Brain 1932 LV 181

177 GRINKER R R and BASSOE P Disseminated encephalomyelitis its relation to other infections of the nervous system Arch Neurol and Psychiat 1931 XXV 7-3

178 McALPINE D Acute disseminated encephalomyelitis its sequelae and its relationship to disseminated sclerosis Lancet 1931 I 846

Encephalitis Following Mumps

05 JOHNSON C D and GOODPASTURE E W An investigation of the etiology of mumps Jour Exp Med 1934 LIX 1
206 HOLDEN E M EAGLES A Y and STEVENS J E Jr Mumps involvement of the central nervous system Jour Am Med Assoc 1946 CXXXI 382
07 KANE L W ENDERS J F COHEN S and LEVENS J H Immunity in mumps I II III Jour Exp Med 1945 LXXXI 93

Encephalitis Accompanying Infectious Mononucleosis

208 JOHANSEN A H Serous meningitis and infectious mononucleosis Acta Med Scandinav 1931 LXXVI 69
09 EPSTEIN S H and DAMESHEK W Involvement of the central nervous system in a case of glandular fever New Eng Jour Med 1931 CCV, 1-38
10 GELFEBTER S Acute mononucleosis complicated by encephalo myelitis Lancet 1946 II 753
211 SLADE, J DE R Involvement of the central nervous system in in fectious mononucleosis New Eng Jour Med 1946 CCXXXIV 753
212 THOMSEN S and VIMTRUP B Lethale tilfalde af mononucleosis infectiosa Nord Med 1939 IV 3295 quoted by Slade see reference no 211
213 RICKER W BLUMBERG A PETERS C H and WIDERMAN A The association of the Guillain Barre syndrome with infectious mononucleosis Blood 1947 II 217

Encephalitis Following Whooping Cough

214 HABEL, K and LUCCHESI P F Convulsions complicating pertussis Am Jour Dis Child 1938 LVI 275

The Russian Spring-Summer Tick Borne Encephalitis

215 SMORODINTSEFF A A The spring summer tick borne encephalitis Arch f d gesamt Virusforchung 1939 40 I 468
216 CASALS J Immunological relationships among central nervous system viruses Jour Exp Med 1944 LXXIX 341

Post Vaccinal Encephalitis

192 LUCKSCH F Blatternimpfung und Encephalitis, Med Klin 19 4, XX 1170

193 BASTIAANSE, F S Encephalite consecutive a la vaccination anti variolique Bull Acad de Med 19 5 XCIV 815 abstracted in Jour Am Med Assoc 19 5 LXXXV 779

194 TURNBULL H M and McINTOSH J Encephalomyelitis following vaccination Brit Jour Exp Path 19 6 VII 181

195 RIVERS T M and SCHWENTKER F F Encephalomyelitis accompanied by myelin destruction experimentally produced in monkeys Jour Exp Med 1935 LXI 689

196 GORDON M H Vaccination and encephalitis British Med Jour 1931 I 155

197 McINTOSH J and SCARFF R W The reaction of the central nervous system to vaccinia virus Jour Path and Bacteriol 1930 XXXIII 483

198 BOUMAN L Impfenzephalitis in Holland Deutsch Zeitschr f Nervenheill 1930 CXVI 169

199 MATSUDA M Experimentelle Studie uber die sogenante post vaccinale Encephalomyelitis Trans Japan Path Soc 19 9 XIX 4-8 abstracted in Zentralbl f d ges Neurol u Psychiat 1930 LVI 790

200 PERDRAU J R The histology of post-vaccinal encephalitis Jour Path and Bacteriol 1928 XXXI 17

201 FINLEY K H Pathogenesis of encephalitis occurring with vaccination variola and measles Arch Neurol and Psychiat 1938, XXXIX 1047

Encephalitis Following Chicken Pox

202 UNDERWOOD E A The neurological complications of varicella a clinical and epidemiological study Brit Jour Child Dis 1935 XXXII 83

203 BULLOWA J G M and WISHIK S M Complications of varicella Am Jour Dis Child 1935 XLIX 923

204 LOWRY E C Chicken pox encephalitis Journal Lancet 1945, LXV 191

229 MEZERA R A BROWN G O MUETHER R O and LEGIER M Intragastric and intraintestinal inoculations with St Louis encephalitis virus Proceed Soc Exp Biol and Med 1941 XLVIII 357

230 BLATTNER R J and HEYS F M Experimental transmission of St Louis encephalitis to white Swiss mice by Dermacentor variabilis Proceed Soc Exp Biol and Med 1941 XLVIII 707

231 BLATTNER R J and HEYS F M Isolation of St Louis encephalitis virus from peripheral blood of human subject Jour Pediat 1946 XXVIII 401

232 HAMMON W McD GRAY J EVANS C and IZUMI E M Western equine and St Louis encephalitis antibodies in the sera of mamals and birds from an endemic area Science 1941 XCIV 305

233 HAMMON W McD and REEVES W Culex tarsalis coq a proven vector of St Louis encephalitis Proceed Soc Exp Biol and Med 194 L 143

234 HAMMON W McD REEVES W C and IZUMI E M St Louis encephalitis virus in the blood of experimentally inoculated fowls and mammals Jour Exp Med 1946 LXXXIII 175

235 HAMMON W McD and REEVES W C Laboratory transmission of St Louis encephalitis virus by three genera of mosquitoes Jour Exp Med 1943 LXXVIII 241

236 SMITH M G BLATTNER R and HEYS F The isolation of the St Louis encephalitis virus from chicken mites (Dermanyssus gallinae) in nature Science 1944 C 36

237 PERDRAU J R The Australian epidemic of encephalomyelitis (x disease) Jour Path and Bacteriol 1936 XLII 59

238 DALLDORF G JUNGEBLUT C W and UMPHLET M D Multiple cases of Choriomeningitis in apartment harboring infected mice Jour Am Med Assoc 1946 CXXXI 25

239 OLITSKY P K and SAENZ A C Serum treatment of western equine encephalitis in mice determined by the course of viral infection Proceed Soc Exp Biol and Med 1948 LXVIII 00

240 SMITHBURN K C HUGHES T P BURKE A W and PAUL J H A neurotropic virus isolated from the blood of a native of *Uganda Am Jour Trop Med* 1940 XX 471

241 BERGER F M and SCHWARTZ R P Oral myanesin in treatment of spastic and hyperkinetic disorders Jour Am Med Assoc 1948 CXXXVII 772

242 PHILIP C B COX H R and FOUNTAIN J H Protective antibodies against St Louis encephalitis virus in serum of horses and man Pub Health Rep 1941 LVI 1388

217 SILBER, L A and SHUBLADZE A K Louping ill in the U S S R Am Rev Soviet Med 1944-45, II 339

218 CASALS J and OLITSKY P K Enduring immunity following vaccination with formalin inactivated virus of Russian spring summer (far eastern tick borne) encephalitis Jour Exp Med, 1945, LXXXII 431

Miscellaneous Additional References

219 BREED R S MURRAY L G D and HITCHINS, A P Bergey s Manual of Determinative Bacteriology 6th Edition Williams and Wilkins Co Baltimore 1948

220 DIMSDALE H Changes in the parkinsonian syndrome in the twentieth century Quart Jour Med 1946 XV 155

221 EVANS A C and FREEMAN W Studies on the etiology of epidemic encephalitis Pub Health Rep 19 7 XLII 171

222 BUCY P C and CASE T J Tremor physiologic mechanism and abolition by surgical means Arch Neurol and Psychiat 1939 XLI 721

223 KLEMME R M Surgical treatment of dystonia with report of 100 cases in Diseases of the Basal Ganglia Assoc for Research in Nerv and Ment Dis Baltimore 1941 XXI 596

224 KLEMME R M The neural mechanism and clinical results of more than oo cases of paralysis agitans Bull St Louis Med Soc 1943 XXXVII 172

225 PUTNAM T J Treatment of unilateral paralysis agitans by section of the pyramidal tract Arch Neurol and Psychiat 1940 XLIV 950

226 MYERSON A and BERLIN O D Case of postencephalitic Parkinson s disease treated by total thyroidectomy New Eng Jour Med 1934 CCX 1205

227 BROUN, G O MUETHER R O MEZERA R A and LEGIER M Transmission of St Louis encephalitis to the hamster, Proceed Soc Exp Biol and Med 1941 XLVI 601

228 BROUN G O LEGIER M MEZERA R A and MUETHER R O Immunological reactions of the hamster to inoculations with the virus of St Louis encephalitis Proceed Soc Exp Biol and Med 1941 XLVIII 310

CHAPTER III-A

POST-VACCINAL ENCEPHALITIS

By A. H. GORDON

TABLE OF CONTENTS

INCIDENCE

The history of post vaccinal encephalitis as a clinical entity does not go back more than two decades. Occasional complications in the central nervous system following vaccination had been noted from time to time and some of these had been diagnosed as tetanus and quite possibly some of them were but in 1912 Turnbull and McIntosh recorded the first case of post vaccinal encephalitis from the London Hospital and between 1912 and 1923 reported six other cases

From 1923 to 1927 in the Netherlands 139 cases of disease of the central nervous system following vaccination had been described of which 41 died. In England the Rolleston committee on vaccination reported 25 cases of acute nervous disease occurring within four weeks of vaccination between January 1 1926 and September 30 1927. Up to May 1929 it was estimated by Jitta that the total number of cases recognized in Holland was 146 and up to September 1929 115 cases had occurred in England

In Germany up to the same date 67 cases had occurred. In Austria 81 cases in France 5 while Belgium Spain Greece and Italy reported no cases Norway had 28 cases Poland [illegible] cases Sweden 16 cases. The Soviet republic reported 2 cases and Jugo-Slavia one case. Asia and Africa reported no cases

For the United States there is a record of 71 probable or proven cases of

243 HAMMON W McD REEVES W BRENNER S and BROOKMAN B Human encephalitis in the Yakima valley, Washington 194 Jour Am Med Assoc, 1945 CXXVIII, 1133
244 HAMMON W McD Eastern and western equine encephalomyelitis and the St Louis type as observed in Washington Arizona New Mexico and Texas Jour Am Med Assoc 1943 CXXI, 560
245 CASALS J and PALACIOS R Complement fixation in encephalitis and rabies virus infections Science, 1941 XCIII 162
246 IKEI S Experimentalle Studien uber das Entstehungsmoment der Postvaccinal encephalitis Japan Jour Exper Med 1932 X 563
247 HIRST G K The quantitative determination of influenza virus and antibodies by means of red cell agglutination Jour Exp Med 194 LXXV 49

July 1 1950

phenomenon was elicited On the following day the knee jerks could not be obtained

There was incontinence of both urine and fæces

On admission there was herpes on both lips The pul e rate was 90 the respirations 16 and the temperature which was 100 2° F on admission rose steadily to 107° F before death two days later

The right arm and leg developed a marked degree of spa m and a lateral nystagmus appeared Later the spasm passed into flaccidity and complete unconsciousness developed

Respirations became more rapid and dulness and rales appeared at the bases of both lungs For some time before death the head and eyes were turned toward the right and both pupils became much contracted

Lumbar puncture on two occasions gave a clear fluid not under tension containing no cells and only a faint reaction for globulin and a negative reaction for sugar Culture of the fluid was negative

Blood examination showed hemoglobin 75 per cent red cells 4 800 000 *leucocytes on three counts 8000 7,00 and ,800 per cu mm*

Vaccination history — The family had recently removed from another Province and as the child had not been vaccinated he could not enter school Twelve days before the onset of the illness vaccination by the scratch method was done in one area on the left arm

On admission the scab which was hard and dark brown, was about 2 cm in diameter with quite marked redness and induration about it The left axillary glands were enlarged and tender

The progress notes upon the case are of interest On the day of admission the following note wa made The ca e has all the appearances of a meningeal reaction but the character is hemiplegic and the predominance of weakness over rigidity is noticeable This with the practically negative spinal fluid suggests some unusual cerebral infection and vaccinia is suggested

The diagnosis made shortly before death was as follows Some type of spreading encephalitis poliomyelitis superior is suggested, with the predominant lesion in the left cortex Terminal bronchopneumonia The terminal myo is and fixed pupils suggest a basal lesion

Necropsy — A very limited post mortem examination was performed ½ hours after death Permission could not be obtained to examine the brain The spinal cord could be examined only from the third cervical to the lumbar region

Many microscopic sections were examined from various areas in the cord The following is the histologic report upon them

Some of the sections show a quite normal condition the neuroglia is intact the vessels are normal the nerve cells dendrites and nerve fibrils are

post vaccinal encephalitis for the ten years prior to 1932, including 2[illegible] cases recorded for 1930 and 8 cases for 1931 In Canada no cases had been reported up to 1930 but two cases are now on record

Clinical Features

The clinical features of the disease form a fairly constant picture and while there is still difference of opinion as to the essential nature and direct cause of the processes involved there is a notable constancy in the manner of onset and the course of the symptoms

The onset is sudden and stormy with headache vomiting, fever and often convulsions Paralysis and coma are frequent Meningeal signs and cranial nerve palsies are commonly present while the cerebrospinal fluid is remarkable for its slight departures from the normal Globulin may or may not be increased The cells are not usually increased greatly in number and the pressure is not elevated

Illustrative Cases

The following two cases illustrate the clinical features

Case 1 A boy aged 11 years who had been well and strong up to the onset of this illness was brought into the Montreal General Hospital unconscious on August 11 1928

He had mumps measles and chickenpox in infancy, otherwise his history was negative

The parents stated that he had been suddenly seized with a severe headache on a Sunday night and that this had continued throughout Monday and Tuesday and was accompanied by vomiting On Wednesday morning he became unconscious and was brought to the hospital

When seen he could be partially aroused but would not answer questions He lay on his left side with his head bent forward and both hips and knees flexed He was restless and every 5 minutes or so would throw himself about in bed

The pupils reacted sluggishly to light the left was somewhat dilated and there was ptosis of the left eyelid

The eyes were kept partially open and responded but little to stimuli There was no disease found in the ears or in the mastoid regions and there was no sign of head injury The ocular fundi were normal

There was some spasticity of both arms and legs the neck was somewhat rigid and Kernig s sign was slightly present The abdominal reflexes were absent the knee jerks were present and a well defined bilateral Babinski

Headache disappeared at the end of the first week but reappeared for a time after several days absence

Blood examination showed red cells 4 400 000 leucocytes 6,400, Hg 90 per cent polynuclears 57 lymphocytes 38 mononuclears 4 per cent

Lumbar puncture was done on six occasions Globulin was constantly present Total protein 075% Sugar 061 The cells averaged 10 chiefly mononuclears The pressure ranged from 80 to 130 mm water

The blood Wasserman the spinal fluid Wasserman and the colloidal gold reaction were negative Blood cultures and culture from the cerebrospinal fluid were negative

On admission the blood sugar was 135 and dropped to 117 at discharge and twice during his illness sugar was found in the urine He was given daily on three successive days o c c of serum from recently vaccinated persons

The temperature fell to normal on the 10th day of the illness and the patient was discharged well in four weeks with slight left facial weakness and deviation of the tongue to the left as the only residual symptoms

Two rabbits were given intracerebral inoculations one with 3 c c of cerebrospinal fluid from this case and the other with vaccine virus in saline solution Both animals survived The one inoculated with cerebrospinal fluid from the patient showing no illness the one inoculated with vaccinia virus becoming ill for a few days

Pathology

The lesions found in post vaccinal encephalitis fall into the category of non suppurative diseases of the central nervous system among which are also included encephalitis lethargica and poliomyelitis While all three show some resemblances they also have marked differences in their histological appearances

With the encephalitis associated with measles variola anti rabies inoculation Schilder s disease and possibly influenza the post vaccinal process has a marked resemblance and some claim an identity

Turnbull and McIntosh sum up the matter by stating that the characteristic features of the inflammation of the central nervous system in post vaccinal encephalitis are the number and size of zones of extra adventitial perivascular infiltration in contrast to the development and size of the adventitial vascular sleeves the obvious perivascular distribution of the infiltrations the conspicuous zones of softening with relatively little cellular infiltration that surround vessels in the white matter the large extent to which the white matter is involved although the involvement of the gray matter is absolutely greater the extensive involvement of both cerebral cortex and spinal cord the incidence

well preserved There are areas in the cord, however, which show lesions of varying intensity in the cord substance There are numerous areas more marked in one half of the cord than in the other, where demyelinization is very prominent These areas appear as discrete and confluent patches In the discrete areas one notes that this lesion occurs as a ring like area about a blood vessel The demyelinization is more marked throughout the anterior portion of the cord than in the posterior portion In some of the sections a similar lesion is seen along each side of the anterior commisure as a zone of varying length and breadth As a whole there is not much cellular infiltration of the demyelinized areas In certain places however, these areas do show quite a marked infiltration with cells

The other organs of the body showed no gross lesion except in the lungs, where congestion and areas of acute bronchopneumonia were found

Microscopically, there was a general vascular congestion of the kidneys, particularly marked in the medulla The convoluted tubules showed cloudy swelling

Sections of the excised vaccination area showed superficial ulceration and a scab consisting of necrotic material Extending through the skin and into the subcutaneous tissue there was a diffuse inflammatory exudate with necrotic foci The cellular exudate was composed of lymphocytes plasma cells, endothelial cells and enormous numbers of eosinophiles

Case 2 A man of 24 years of age who had three times been vaccinated, but in whom vaccination had never taken and who showed no scar was vaccinated again on January 1 1932 by a physician of the Board of Health

Three days later his arm became very sore and inflamed and on January 27, six days later he suddenly developed headache and photophobia vomited repeatedly and could not sleep

He was seen by Dr W R Kennedy who found marked retraction of the neck and slight temperature and did a lumbar puncture The fluid returned clear with an increase of globulin but no increase of cells In view of the history and the findings he made a diagnosis of post vaccinal encephalitis and the man was admitted to the Montreal General Hospital The pulse was 84, temperature 99 2° F blood pressure 140/100

The head was drawn back and the neck rigid and there was a marked Kernig reaction The pupils were even and reacted to light There was a lateral nystagmus on looking to the right but there was no ocular palsy There was soreness in the muscles of mastication and he objected to opening his mouth which raised the suspicion of tetanus

There was distinct weakness of the lower left face with loss of sensation and later weakness of the left arm appeared The left abdominal reflex was diminished The ocular fundi showed no change

Headache disappeared at the end of the first week but reappeared for a time after several days absence

Blood examination showed red cells 4,400 000 leucocytes 6 400 Hg 90 per cent polynuclears 54 lymphocytes 38 mononuclears 4 per cent

Lumbar puncture was done on six occasions Globulin was constantly present Total protein 0,5% Sugar 061 The cells averaged 10 chiefly mononuclears The pressure ranged from 80 to 130 mm water

The blood Wasserman the spinal fluid Wasserman and the colloidal gold reaction were negative Blood cultures and culture from the cerebrospinal fluid were negative

On admission the blood sugar was 135 and dropped to 117 at discharge and twice during his illness sugar was found in the urine He was given daily on three successive days o c c of serum from recently vaccinated persons

The temperature fell to normal on the 10th day of the illness and the patient was discharged well in four weeks with slight left facial weakness and deviation of the tongue to the left as the only residual symptoms

Two rabbits were given intracerebral inoculations one with 3 c c of cerebrospinal fluid from this case and the other with vaccine virus in saline solution Both animals survived The one inoculated with cerebrospinal fluid from the patient showing no illness the one inoculated with vaccinia virus becoming ill for a few days

Pathology

The lesions found in post vaccinal encephalitis fall into the category of non suppurative diseases of the central nervous system among which are also included encephalitis lethargica and poliomyelitis While all three show some resemblances they also have marked differences in their histological appearances

With the encephalitis associated with measles variola anti rabies inoculation Schilder s disease and possibly influenza the post vaccinal process has a marked resemblance and some claim an identity

Turnbull and McIntosh sum up the matter by stating that the characteristic features of the inflammation of the central nervous system in post vaccinal encephalitis are the number and size of zones of extra adventitial perivascular infiltration in contrast to the development and size of the adventitial vascular sleeves the obvious perivascular distribution of the infiltrations the conspicuous zones of softening with relatively little cellular infiltration that surround vessels in the white matter the large extent to which the white matter is involved although the involvement of the gray matter is absolutely greater the extensive involvement of both cerebral cortex and spinal cord the incidence

of the maximal inflammation upon the lumbar and upper sacral cord and the pons, and the close similarity in the type and incidence of the inflammation in all cases The most characteristic histological feature is the zone of perivascular softening in the white matter

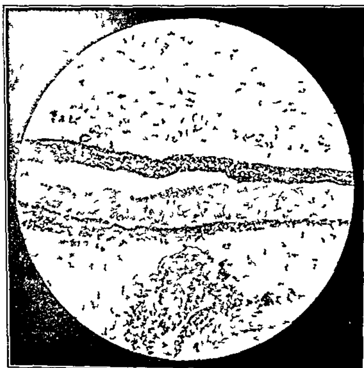


FIG 1 — Encephalitis Lethargica Broad lymphatic collar about a small cerebral vessel

There are certain aspects of the microscopic lesions of poliomyelitis post vaccinal encephalitis and encephalitis lethargica that are similar yet there are certain lesions which seem to differentiate these three disease The accompanying illustrations demonstrate especially these differentiating features

Fig 1 is from a clinical case of encephalitis lethargica It shows a blood vessel dilated with blood About it is a very distinct encircling zone infiltrated with cells most of which are of the lymphocytic series The slide shows this alone None of the areas of softening that have been described in encephalitis lethargica are present Perivascular lymphocytic collars are not diagnostic of encephalitis because they appear in other acute diseases of the central nervous system one of which is post vaccinal encephalitis

Fig 2 is from a clinical case of anterior poliomyelitis The microphotograph

is taken so as to include a portion of the anterior horn and the adjacent white matter One intact motor nerve cell and the sites of two others are seen The latter areas contain numerous phagocytic cells which have almost completely removed the two nerve cells that have been destroyed by the virus of polio-

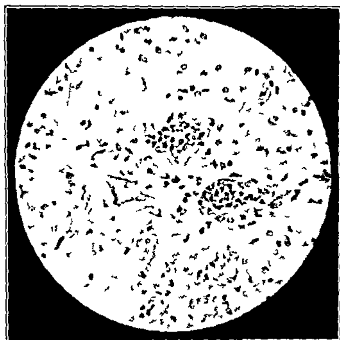


Fig 2 — Anterior Poliomyelitis Portion of anterior horn with adjacent white matter to show one nerve cell intact the sites to two others are represented by great numbers of phagocytic cell Note the absence of demyelinization

myelitis There is no demyelinization This lesion has not been described in association with post vaccinal encephalitis

Fig 3 is from the first case of post vaccinal encephalitis This shows the microscopic lesion which is said to be characteristic of the disease areas of demyelinization In this particular case these areas are more numerous in one half of the cord are discrete and confluent and in the centre of some of them a dilated and engorged blood vessel is distinctly seen

Fig 4 from the same case and near the same site as Fig 3 shows very marked demyelinization and like the former slide there are dilated vessels with areas of demyelinization about them

of the maximal inflammation upon the lumbar and upper sacral cord and the pons and the close similarity in the type and incidence of the inflammation in all cases The most characteristic histological feature is the zone of perivascular softening in the white matter

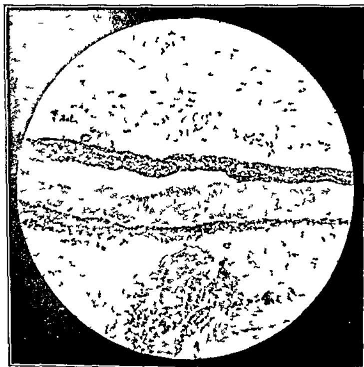


Fig 1 — Encephalitis Lethargica Broad lymphatic collar about a small cerebral vessel

There are certain aspects of the microscopic lesions of poliomyelitis post vaccinal encephalitis and encephalitis lethargica that are similar, yet there are certain lesions which seem to differentiate these three diseases The accompanying illustrations demonstrate especially these differentiating features

Fig 1 is from a clinical case of encephalitis lethargica It shows a blood vessel dilated with blood About it is a very distinct encircling zone infiltrated with cells most of which are of the lymphocytic series The slide shows this alone None of the areas of softening that have been described in encephalitis lethargica are present Perivascular lymphocytic collars are not diagnostic of encephalitis because they appear in other acute diseases of the central nervous system, one of which is post vaccinal encephalitis

Fig 2 is from a clinical case of anterior poliomyelitis The microphotograph

is taken so as to include a portion of the anterior horn and the adjacent white matter One intact motor nerve cell and the sites of two others are seen The latter areas contain numerous phagocytic cells which have almost completely removed the two nerve cells that have been destroyed by the virus of polio-

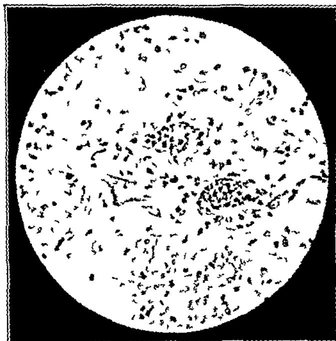


Fig 2 — Anterior Poliomyelitis Portion of anterior horn with adjacent white matter to show one nerve cell intact the sites to two others are represented by great numbers of phagocytic cel Note the absence of demyelinization

myelitis There is no demyelinization This lesion has not been described in association with post vaccinal encephalitis

Fig 3 is from the first case of post vaccinal encephalitis This shows the microscopic lesion which is said to be characteristic of the disease areas of demyelinization In this particular case these areas are more numerous in one half of the cord are discrete and confluent and in the centre of some of them a dilated and engorged blood vessel is distinctly seen

Fig 4 from the same case and near the same site as Fig 3 shows very marked demyelinization and like the former slide there are dilated vessels with areas of demyelinization about them

of the maximal inflammation upon the lumbar and upper sacral cord and the pons, and the close similarity in the type and incidence of the inflammation in all cases The most characteristic histological feature is the zone of perivascular softening in the white matter

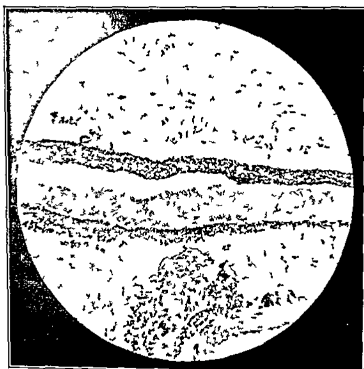


Fig 1 — Encephalitis Lethargica Broad lymphatic collar about a small cerebral vessel

There are certain aspects of the microscopic lesions of poliomyelitis, post vaccinal encephalitis and encephalitis lethargica that are similar yet there are certain lesions which seem to differentiate these three diseases The accompanying illustrations demonstrate especially these differentiating features

Fig 1 is from a clinical case of encephalitis lethargica It shows a blood vessel dilated with blood About it is a very distinct encircling zone infiltrated with cells most of which are of the lymphocytic series The slide shows this alone None of the areas of softening that have been described in encephalitis lethargica are present Perivascular lymphocytic collars are not diagnostic of encephalitis because they appear in other acute diseases of the central nervous system, one of which is post vaccinal encephalitis

Fig 2 is from a clinical case of anterior poliomyelitis The microphotograph

adventitial softening and the lesions have the punched out appearance of those in disseminated sclerosis Thus demyelinization appears to be the primary lesion and cellular infiltration is secondary

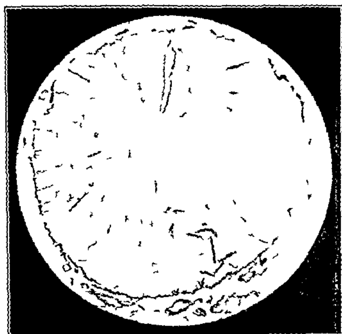


FIG 4 — Post vaccinal Encephalitis Transverse section of cord showing demyelinization most marked throughout one half of the cord

RELATION TO VACCINATION

In the 90 English cases the period elapsing between the date of vaccination and the onset of encephalitis was in 81 cases from the 7th to the 15th day with the greatest number on the 12th day Eight cases appeared up to the 6th day and one on the 3rd day

In this group of 90 cases collected by the Committee on Vaccination in 1927 and 1928 there were 4 deaths of these 41 occurred within 3 weeks of the onset

Two thirds of the cases were of school age and all the vaccinations were primary except in 3 of the 90 cases The age group from 4 years to 15 years furnished 68 cases or 75 per cent

Of the 41 fatal cases in this group 31 or 75 per cent occurred in the same

Fig 5, also from this case of post vaccinal encephalitis, is a high power photograph of a small area of demyelinization in the grey matter It shows infiltration of an area of demyelinization with cells

Figs 3 4 and 5 demonstrate the microscopic lesions which are claimed by Turnbull and others to be characteristic of post vaccinal encephalitis.

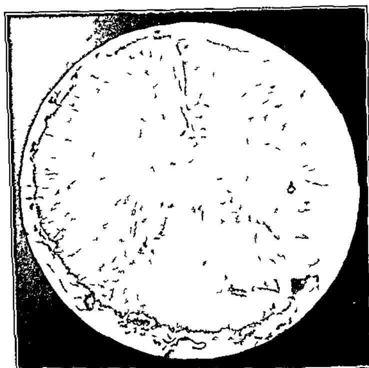


Fig 3 — Post vaccinal Encephalitis To illustrate areas of demyelinization in the centres of some of which a widely dilated blood vessel is seen

Microscopically the general character of the lesion of post vaccinal encephalitis is that of a meningo-encephalitis The meninges are infiltrated with small lymphocytes plasma cells and large cells of endothelial origin While the meningitis is slight it can be traced down over the cord

Infiltration of the perivascular space the so-called lymphocytic collar or sleeve of the type seen in epidemic encephalitis is the commonest lesion present, but this feature is shared with both epidemic encephalitis and poliomyelitis The striking feature of the post vaccinal disease is the presence of areas of demyelinization extending for some distance around the vessels and unassociated with vascular thrombosis Demyelinization is an essential feature of the extra

vaccinations had been done in children under one year no cases of encephalitis had occurred

In this connection it should be noted that T. I. McNair Scott reports a case in a child of 6 months occurring 10 days after vaccination and recovering in 16 days. He also reports 1 other cases from various sources but many of these vary from the usual picture of the disease both in time of onset and clinical course so that one must still regard vaccinal encephalitis as excessively rare in infancy

A study of combined statistics would justify the broad statement that post vaccinal encephalitis is in general a disease following primary vaccination in children between 6 and 1 years of age

The relation of the onset of encephalitis to the number of insertions and to the intensity of the vaccination reaction is not easy to determine

The great majority of the English cases followed vaccination in 4 insertions but as the Rolleston report comments there were more vaccinations in four insertions than in 3 and 1 insertions combined but it is of interest that in 1929 public vaccinators were ordered to make one insertion only

The same uncertainty holds as to the relation of encephalitis to the intensity of the vaccination reaction though a perusal of case reports indicates that severe reactions have been common events in those stricken by encephalitis

ETIOLOGY

Many questions remain to be answered in reference to the disease as a whole and the problem is well presented by Turnbull and McIntosh

They state that three possibilities appear

1 That vaccination provokes a virus already present in the body The presence of almost identical findings in the nervous system in measles small pox anti rabic inoculation etc would offer some support for this view

That the vaccination lymph is contaminated

3 That some other virus contaminates the vaccination wound

The fact that the disease has followed vaccination with lymphs from various sources in the same epidemic is an argument against the two last views

Their conclusion is that the clinical and histological features of the disease are so constant that there can be little doubt that vaccination is not a coincidence but a cause of the encephalitis

In this connection it may be noted that Alderhoff of Holland puts forward the view that a monilia often found in the throats of cases of encephalitis and of poliomyelitis as well as in the throats of contacts may be the responsible virus

From the standpoint of epidemology there is no correlation between the

age group of 4 to 15 In this whole group of 90 cases, no case occurred in the period up to one year of age

In the Bulletin of the Office International d'Hygiene Publique of 1930

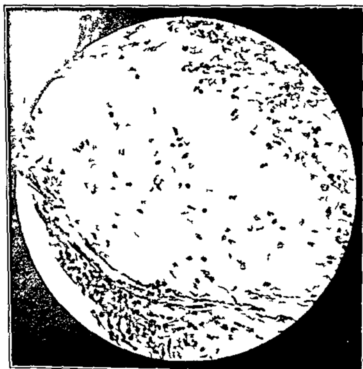


FIG 5 — Post vaccinal Encephalitis Cellular infiltration in an area of demyelinization High power

XXII which is a report of the Smallpox and Vaccination Commission, the figures relating to the disease in the Netherlands are in general similar to the English statistics Eighty three cases of encephalitis following vaccination are tabulated of which 52 occurred after primary vaccination and 31 after re vaccination Of these attacked after primary vaccination 14 died or 26 9 per cent

On an average the symptoms appeared on the 11th or 12th day, while after revaccination the average onset was on the 10th day but sometimes even on the 2nd day, and on the average death occurred on the 5th day

It was calculated that one case of encephalitis occurred in every - 300 primary vaccinations and one in every 50 000 revaccinations One case occurred among 3 487 children vaccinated between 1 and 2 years of age and one case in every 815 primary vaccinations between 6 to 11 years and though 16 000

vaccinations had been done in children under one year no cases of encephalitis had occurred.

In this connection it should be noted that T. T. McNair Scott reports a case in a child of 6 months occurring 10 days after vaccination and recovering in 16 days. He also reports 21 other cases from various sources but many of these vary from the usual picture of the disease both in time of onset and clinical course so that one must still regard vaccinal encephalitis as excessively rare in infancy.

A study of combined statistics would justify the broad statement that post vaccinal encephalitis is in general a disease following primary vaccination in children between 6 and 1[illegible] years of age.

The relation of the onset of encephalitis to the number of insertions and to the intensity of the vaccination reaction is not easy to determine.

The great majority of the English cases followed vaccination in 4 insertions but as the Rolleston report comments there were more vaccinations in four insertions than in 3, [illegible] and 1 insertions combined but it is of interest that in 1929 public vaccinators were ordered to make one insertion only.

The same uncertainty holds as to the relation of encephalitis to the intensity of the vaccination reaction though a perusal of case reports indicates that severe reactions have been common events in those stricken by encephalitis.

ETIOLOGY

Many questions remain to be answered in reference to the disease as a whole and the problem is well presented by Turnbull and McIntosh.

They state that three possibilities appear:

1 That vaccination provokes a virus already present in the body. The presence of almost identical findings in the nervous system in measles small pox anti rabies inoculation etc would offer some support for this view.

2 That the vaccination lymph is contaminated.

3 That some other virus contaminates the vaccination wound.

The fact that the disease has followed vaccination with lymphs from various sources in the same epidemic is an argument against the two last views.

Their conclusion is that the clinical and histological features of the disease are so constant that there can be little doubt that vaccination is not a coincidence but a cause of the encephalitis.

In this connection it may be noted that Aldershoff of Holland puts forward the view that a monilia often found in the throats of cases of encephalitis and of poliomyelitis as well as in the throats of contacts may be the responsible virus.

From the standpoint of epidemology there is no correlation between the

incidence of this disease and the incidence of encephalitis lethargica or of poliomyelitis but there is a direct correlation between it and the number of cases of smallpox and the number of charges of vaccine lymph distributed by the Health Boards

All attempts have so far failed to reproduce encephalitis in animals by the injection of material from the brains of those dying of the disease

In spite of this Hekman of Rotterdam is unwilling to admit that an unknown virus is responsible for the disease and strongly upholds the view that vaccinia alone is the responsible agent and he supports this view by reports of 11 cases of encephalitis following vaccination and 2 following revaccination which were treated by the injection of blood serum from recently vaccinated persons Of these 13 cases 11 recovered

Netter strongly supported Hekman s views and on this basis also Professor Paschen Director of the Vaccination Institute of Hamburg arranged for the collection of blood from recently vaccinated nursing students for the early treatment of cases of post vaccinal nervous disease

Unknown to Hekman at the time Sir Thomas Horder in London had reported a case of vaccinal encephalitis treated successfully at St Bartholomew s Hospital by intrathecal injection of serum from the patient s mother who had been recently vaccinated

Treatment

The treatment of post vaccinal encephalitis should follow the lines employed in other forms of encephalitis Lumbar puncture repeated daily if need be has justified itself and in the second of our cases it gave so much relief to the headache that the patient himself requested it

Sedatives as codein and morphin may be required, and quiet and relative darkness help to make the patient comfortable

While by some regarded as empirical and by others as valueless the injection of the serum of recently vaccinated persons particularly those vaccinated by the same type of vaccine has a reasonable basis and in view of Hekman s results is amply justified It may be given intravenously or intrathecally in doses of 10 to 50 c c daily

Where time is a factor and no such prepared serum is available, the intramuscular injection of the donor s citrated whole blood may be employed It should be given at the very first appearance of central nervous symptoms which appear within the incubation period of post vaccinal encephalitis

In larger institutions a supply of serum might be obtained from recently vaccinated people such as entrants into the schools for nurses after the plan of Paschen

This continent has had its occasional cases and with a large unvaccinated population the appearance of an epidemic of smallpox or a smallpox scare which would lead to mass primary vaccination at the susceptible age periods might readily duplicate the experience of the European countries, with regard to post vaccinal encephalitis

Prevention

In the matter of prevention it is beyond argument that in Europe it is the countries in which early vaccination has not been compulsory which have suffered most from this disease

Whatever arguments there may be about the exact nature of the infecting agent there is no argument about the fact that the disease is a rarity in children vaccinated under one year of age Therefore the first step toward prevention is early vaccination

The Rolleston Commission was sufficiently impressed by the greater danger of encephalitis in those vaccinated by four insertions to recommend that only one insertion be employed and this method is now compulsory with public vaccinators in England It is also realized that dilution of vaccine lymph to the greatest degree compatible with activity is a wise precaution

Finally every effort must be made to develop a method of protection against smallpox without the use of a living virus

BIBLIOGRAPHY

ALDERSHOFF H Recherches sur la cause de l encephalite postvaccinale Bulletin de l Acad de Med Paris 1930 CIII 533
ARMSTRONG C Post vaccination encephalitis Annals Int Med 1931 V 332
BRADFORD J R and BASHFORD E F Acute infective polyneuritis Quart Jour Med 1919 XII 88
BROWN C L and SYMMERS D Acute serous encephalitis Am. Jour Dis Child. 1925 XLVII 174
COLLIER J and GREENFIELD J G The encephalitis periaxialis of Schilder Brain 1924 XLVII 489
DONNELLY H H Vaccinal encephalomyelitis Jour Allergy 1931 II 396
FLEXNER S Epidemic (lethargic) encephalitis and allied conditions Jour Am Med Assoc 1923 LXXXI 1688
FLEXNER S Postvaccinal encephalitis Trans Assoc. Am Phys 1929 XLIV 181
FLEXNER S Postvaccinal encephalitis and allied conditions Jour Am Med Assoc 1930 XCIV 305

GORDON A H Post vaccinal encephalitis Trans Assoc Am Phys 1931 XLVI 188

GRINKER R R and SONIE I I Acute toxic encephalitis in childhood Arch Neurol and Psychiat 1928 XX 244

HEKMAN J L encephalite post vaccinale et son traitement par le serum homologue Bull de l Academie de Med Paris 1930 CIII 539

HASSIN G B A note on the comparative histopathology of acute anterior poliomyelitis and epidemic encephalitis Arch Neurol and Psychiat 1924 XI 8

HORDER SIR THOS Cerebral symptoms following vaccination rapid recovery after intrathecal injection of post vaccinal serum Lancet 1929 I 1301

MICHELS N A and GLOBUS J H The so called small round cell infiltrations (polioencephalitis and acute epidemic encephalitis) Arch Path 1927 IV 69

MILLER M K Familiar types of encephalitis Jour Am Med Assoc, 1931 XCVII 161

MUSSER J H and HAUSER G H Encephalitis as a complication of measles Jour Am Med Assoc 1928 XC 1267

NETTER M A Discussion — L encephalite post vaccinale et son traitement par le serum homologue Bull de l Academie de Med Paris 1930 CIII 550

PERDRAU J R The histology of postvaccinal encephalitis Jour Path and Bacteriol 1928 XXXI 17

SHELDON W D DOYLE J B and KERNOHAN J W Encephalitis periaxialis diffusa Arch Neurol and Psychiat 1929 XXI 1270

TURNBULL H M and McINTOSH J Encephalomyelitis following vaccination Brit Jour Exper Path 1927 VII 181

SCOTT T F McNAIR Post vaccinal encephalitis Brit Jour Child Dis 1930 XXVII 245

Ministry of Health of Great Britain Report upon vaccination Nov 1930

Editorials Epidemic constitution Lancet 1928 II 33 The risks of vaccination Lancet 1931 I 85

BOYD W M Pathology of Internal Diseases Lea & Febiger Phila 1931

McLURE W B Urticaria and nervous manifestations following vaccination China Med Jour 1930 XLIV 56

WRENCH C T A case of probable post vaccinal encephalitis Indian Med Gaz 1930 LXV 443

ECKSTEIN VON A HERZBERG-KREMMER H and HERZBERG KURT Weitere Beitrage sur Klinik der Vakzinations Enzephalitis Deutsche med Wochenschrift 1930 LVI 1429

VON GRUNEBERG Zur Therapie der Postvaccinalen Encephalitis Klin Wochenschrift 1930 IX 1127

HINRICHS A Enzephalitis nach Vakzination Centralbl fur allg Path u path Anat 1930 XLIX 1

HENNER K Encephalite apres vaccination antivariolique Revue Neurologique 1930 II 418
BELLI C M I Encefalita post vaccinica Rinascenza Medica 1930 July 1 p 305
ESSER A Die Hirnschadigungen nach Pockenschutzimpfung Virchows Archiv 1930 CCLXXVIII 00

Jan 1 1933

CHAPTER IV

BRAIN ABSCESS

By C. M. Hinds Howell

Table of Contents

munder to nasal infection Evans in his series of 194 brain abscesses found that 109 followed infection in the ear and only 1. derived from nasal infection

Brain Abscess Arising from Some Remote Focus of Infection—In these metastatic abscesses the infection is blood borne Of these the lungs furnish the largest number of cases bronchiectasis empyema and purulent bronchitis heading the list whilst abscess of lung gangrene and pneumonia make a smaller contribution

The following table compiled from Evans series shows the relative frequency of the causal factors

Method	*Number of cases*	*Total*
1 Direct extension		
Ear	109	
Nose	1	1 9
Trauma	8	
Spread by bloodstream		
From lung (bronchiectasis	17	
empyema)	5	46
Pyaemia	4	
3 Doubtful or unknown	17	17

In cases of metastatic abscess arising from whatever cause or in cases due to adjacent infection the abscess may be acute or chronic Whereas in cases due to ear or nasal infection there is almost invariably a single abscess in the metastatic cases as might be anticipated either single or multiple abscesses may occur Schorstein[8] recorded 18 cases of metastatic abscess of these 11 were single and 7 multiple Four only of these had a recognizable capsule suggesting some degree of chronicity the remaining 14 were all acute Among 33 additional cases making 51 in all 3 were single and 19 multiple In Evans series of 17 cases 11 were solitary It is probably true to say that at least 50 per cent of metastatic abscesses are single and that the majority of them are acute

Blood borne infection appears to be carried by the middle cerebral artery in the majority of cases the abscess developing more often in the centrum ovale than in any other area

Brain Abscess Arising from Trauma—The frequency with which such cases occur appears to be diminishing apart from war injuries to the skull In Gowers s series quoted by Wilson among 41 cases no less than 4 per cent were regarded as traumatic in origin whilst in Evans

Abscess of the brain was recognized during the eighteenth century but it was not until near the end of the nineteenth that the first cases of successful treatment by surgery were recorded by MacEwen[1] in Glasgow, his work must be regarded as laying the foundations for the present methods of diagnosis and treatment of the condition

With regard to the general incidence of brain abscess Evans found that among 14,354 autopsies at the London Hospital (England) from 1906 to 1925 there were 194 cases The sex incidence shows a preponderating number in males although the reason for this is not obvious The age incidence is greatest in the second and third decades, although no age group is exempt

Etiology

There are three main sources from which abscess in the brain may develop These are (1) from some adjacent focus of infection (2) from some remote focus of infection and (3) from trauma Each of these must now be considered

Brain Abscess Arising from Some Adjacent Focus of Infection — The most common source of infection is suppuration in the middle ear or labyrinth Next in order of frequency come infections of the nasal or paranasal sinuses Much less commonly abscess in the brain may follow septic conditions of the face, scalp or neck such as carbuncles erysipelas cellulitis of orbital tissues and so on Statistics showing the frequency with which suppuration within the cranial cavity has followed infection of the ear have, for the most part, been compiled before the advent of the sulfonamide drugs and penicillin It is almost certain that the introduction of treatment with these drugs will reduce very materially the frequency of intracranial complications of infective ear disease

However some statistics are worth quoting Ruegg[3] found that intracranial complications of ear disease occurred at a Basle clinic 339 times in connection with 25,703 cases of otorrhoea (1.3 per cent) Turner and Reynolds[4], quoting records from the Edinburgh Royal Infirmary found 276 intracranial complications in 11,826 cases of otorrhea (2.3 per cent) Of the possible intracranial complications of infective ear disease abscess in the brain is the least common, among Ruegg's 339 cases only 28 cases of brain abscess occurred That infection in the ear is a more common cause of brain abscess than nasal infection is well recognized Gowers quoted by S A K Wilson[5], found that of 241 brain abscesses 102 were secondary to disease in the ear and a small re-

inferior to nasal infection Evans in his series of 194 brain abscesses found that 109 followed infection in the ear and only 12 derived from nasal infection

Brain Abscess Arising from Some Remote Focus of Infection—In these metastatic abscesses the infection is blood borne Of these the lungs furnish the largest number of cases bronchiectasis, empyema and purulent bronchitis heading the list whilst abscess of lung gangrene and pneumonia make a smaller contribution

The following table compiled from Evans series shows the relative frequency of the causal factors

Method	*Number of cases*	*Total*
1 Direct extension		
Ear	109	
Nose	12	129
Trauma	8	
Spread by bloodstream		
From lung (bronchiectasis	17	
empyema)	5	46
Pyaemia	4	
3 Doubtful or unknown	17	17

In cases of metastatic abscess arising from whatever cause or in cases due to adjacent infection the abscess may be acute or chronic Whereas in cases due to ear or nasal infection there is almost invariably a single abscess in the metastatic cases as might be anticipated either single or multiple abscesses may occur Schorstein[1] recorded 18 cases of metastatic abscess of these 11 were single and 7 multiple Four only of these had a recognizable capsule suggesting some degree of chronicity, the remaining 14 were all acute Among 33 additional cases making 51 in all 3 were single and 19 multiple In Evans' series of 17 cases 11 were solitary It is probably true to say that at least 50 per cent of metastatic abscesses are single and that the majority of them are acute

Blood borne infection appears to be carried by the middle cerebral artery in the majority of cases the abscess developing more often in the centrum ovale than in any other area

Brain Abscess Arising from Trauma—The frequency with which such cases occur appears to be diminishing apart from war injuries to the skull In Gowers series, quoted by Wilson among 241 cases no less than 24 per cent were regarded as traumatic in origin whilst in Evans

series of 194 cases only 8 were so regarded Simple fracture of the skull unless it involves an air sinus, is most unlikely to be followed by abscess formation and contusion of the brain never, so far as I can discover has caused a brain abscess Compound fractures particularly those with indriven fragments of bone or metal, are dangerously likely to cause the development of an abscess, usually within a short space of time but on occasion either months or even years after the injury

Unidentified Brain Abscess —Readers will have noted that in Evans' series of 194 cases there occur 17 cases, nearly 9 per cent, described as of doubtful or unknown origin Although it is probably true to say that primary brain abscess does not occur the actual infection of parts either adjacent or remote may have appeared quite trivial at the time and their incidence have gone unrecorded I have met instances of this in connection with otitic abscess when after the event a history of preceding earache has been recalled perhaps some months earlier and in which almost certainly the ear was the focus from which the abscess derived, another example were one needed of the supreme importance of the necessity for most minute and thorough anamnesis in all cases

Bacteriology —The common pyogenic organisms are those most often found in cerebral abscess particularly streptococci and pneumococci although staphylococci are by no means rare, particularly in children Not rarely the pus in a chronic abscess may be found sterile on culture Among more unusual types *B influenzae*, pneumobacillus *B pyocyaneus*, *B typhosus* and the gonococcus must be mentioned I had under my own care a case in which an actinomycotic abscess was found in each occipital lobe

Pathogenesis and Pathology

Paths of Infection from Adjacent Structures

Atkinson[7] points out that there are three ways in which infection may reach the brain (1) by direct extension through the bone, (2) by vascular channels and (3) by preformed pathways

Infection by Direct Extension Through the Bone —By direct extension from the bone the dura is reached and becomes involved in the inflammatory process In many cases particularly when the infecting agent is not virulent the dura forms a barrier to its further progress It becomes adherent around the edge of the inflammatory area and so

a circumscribed extradural abscess may arise This seems to occur particularly in young subjects and is by no means an uncommon event Of 75 cases of intracranial abscess examined at St Bartholomew s Hospital (England) 43 were extradural, and of these 26 occurred in the first 2 decades of life If the infection is a highly virulent one necrosis of the dura ensues and leptomeningitis will occur with or without the formation of an acute brain abscess In less acute infections the meninges become adherent to the bone and to the surface of the brain the general subarachnoid space is shut off by adhesions and a subacute or chronic brain abscess may result

Passage of Infection by Vascular Channels—Infection may reach the brain substance and cause abscess formation beneath the cortex either by passage along the perivascular space (Virchow-Robin) by retrograde thrombophlebitis or by arterial thrombosis and septic infarction Of these alternative paths infection by the perivascular route appears much the most common In Atkinson s series he was able to trace 81 per cent to this path whilst he found infection by thrombophlebitis twice only in his 16 cases and in only one case had arterial infarction occurred It is perhaps prudent to bear in mind that the difficulties at operation or post mortem of being certain of the method of infection are considerable

Infection by Preformed Pathways—These are potential sources of infection from disease of the ear Three such pathways open on the posterior surface of the petrous bone into the posterior fossa These are (1) internal auditory meatus ( ) aqueduct of vestibule and (3) hiatus subarcuatus Also in close proximity to the petrous bone lies the anterior end of the lateral sinus Infection travelling by any of these routes may cause lateral sinus thrombosis extradural abscess meningitis or cerebellar abscess although infection via the internal auditory meatus is more likely to cause meningitis than abscess formation As one or more of these conditions may occur in addition to abscess formation in the cerebellum the difficulties of accurate diagnosis need no emphasizing

It is important whilst considering possible ways in which infection of adjacent structures may cause abscess in the brain to mention other conditions to which such inflammation may give rise as these will of necessity come under review when discussing the diagnosis of brain abscess Mention has been made already of lateral sinus thrombosis extradural abscess and leptomeningitis There are three other conditions which must now be referred to briefly (1) localized non suppurative encephalitis (2) otitic hydrocephalus and (3) arachnoiditis

Localized Non suppurative Encephalitis

This has been described by a number of observers (Atkinson[7], Symonds[8] Adson[9], Borries[10]) This condition is really indistinguishable from abscess clinically It has been found usually in the temporal lobe secondary to ear infection At operation a softened, inflammatory area of cerebral tissue has been found, but there has been no pus formation The prognosis in such cases appears to be better than is the case with abscess

Otitic Hydrocephalus

This name was suggested by Symonds in 1931, when he reviewed the literature of the subject and added a description of 6 cases which he had observed personally The condition seems to have been mentioned first by Taylor in 1890[11] in the first edition of his textbook, the Practice of Medicine Quincke[12] described cases of increased intracranial pressure with clear cerebrospinal fluid which he included in his category of serous meningitis He attributed the condition to otitis media, head injury overwork influenza and alcoholism Warrington[13] described conditions of intracranial serous effusions of inflammatory origin and noted that there might be an associated hemiparesis Passot[14] described a similar condition observed that the incidence was higher in children than in adults and found it usually associated with otitis media It may occur without other intracranial complications, but there may co exist for example extradural abscess or lateral sinus thrombosis The out standing features of the condition are signs of increased intracranial pressure as shown by the presence of papilloedema, often of very high degree recurrent headaches and vomiting occurring in association with aural infections In the frequent absence of other intracranial complica tions the patient is afebrile There may be a sixth nerve paresis on one or both sides or even a hemiparesis When free from headache the patient is bright, cheerful and mentally alert in marked contrast to the picture presented by a patient with a brain abscess The cerebrospinal fluid is under very great pressure frequently overflowing from the top of the manometer and on examination is found to be quite normal Treatment is best carried out by repeated lumbar puncture but it may take weeks or months for the condition to subside Usually there are no sequelae but optic atrophy may follow occasionally Symonds thought the cause of the condition uncertain It was, he thought due to either an increased

production or diminished absorption of cerebrospinal fluid As there was clearly an excess of fluid he suggested the name of otitic hydrocephalus which seems in my opinion a very adequate description

Arachnoiditis

Arachnoiditis[35] inflammation of the arachnoid causing thickening and adhesions often associated with cystic collection of cerebrospinal fluid is sometimes found in the posterior fossa and may simulate abscess formation This condition has been described also under the title of circumscribed serous meningitis Chronic infection in the ear and petrous bone is the usual cause of this condition but it also occurs in connection with acute infections

Otitic Abscess

Otitic abscess may occur by whatever pathway arising either in the tempero sphenoidal lobe or in the cerebellum and more often in the former than in the latter The following table gives examples —

Author	*Number of Cases*	*Temporal*	*Cerebellar*	*Elsewhere*
Oppenheim	76	55	13	8
St Bartholomew s Hospital London	48	6	2	—
Evans	109	6	40	7
Atkinson	1	1	9	—

The path of infection in cases of abscess in the *temporal lobe* usually is via the tegmen tympani or roof of the attic whilst infection of the labyrinth and lateral sinus usually leads to cerebellar location The middle third of the temporal lobe is the usual area involved whilst the anterior and outer part of the lateral cerebellar hemisphere commonly is involved in subtentorial abscess formation The abscess is almost invariably on the side of the affected ear but cases have been recorded in which a contralateral abscess has occurred In such a case the infection must have been carried by the blood stream Brain abscess may be acute or chronic the determining factors being no doubt time and the virulence of the infecting organism The abscess may be entirely sub

Localized Non suppurative Encephalitis

This has been described by a number of observers (Atkinson[7], Symonds[8], Adson[9], Borries[10]) This condition is really indistinguishable from abscess clinically It has been found usually in the temporal lobe secondary to ear infection At operation a softened inflammatory area of cerebral tissue has been found, but there has been no pus formation The prognosis in such cases appears to be better than is the case with abscess

Otitic Hydrocephalus

This name was suggested by Symonds in 1931, when he reviewed the literature of the subject and added a description of 6 cases which he had observed personally The condition seems to have been mentioned first by Taylor in 1890[11] in the first edition of his textbook, the Practice of Medicine Quincke[1] described cases of increased intracranial pressure with clear cerebrospinal fluid which he included in his category of serous meningitis He attributed the condition to otitis media, head injury overwork, influenza and alcoholism Warrington[13] described conditions of intracranial serous effusions of inflammatory origin and noted that there might be an associated hemiparesis Passot[14] described a similar condition, observed that the incidence was higher in children than in adults and found it usually associated with otitis media It may occur without other intracranial complications, but there may co exist for example extradural abscess or lateral sinus thrombosis The outstanding features of the condition are signs of increased intracranial pressure as shown by the presence of papilloedema, often of very high degree, recurrent headaches and vomiting occurring in association with aural infections In the frequent absence of other intracranial complications the patient is afebrile There may be a sixth nerve paresis on one or both sides or even a hemiparesis When free from headache the patient is bright cheerful and mentally alert in marked contrast to the picture presented by a patient with a brain abscess The cerebrospinal fluid is under very great pressure, frequently overflowing from the top of the manometer and on examination is found to be quite normal Treatment is best carried out by repeated lumbar puncture but it may take weeks or months for the condition to subside Usually there are no sequelae but optic atrophy may follow occasionally Symonds thought the cause of the condition uncertain It was he thought due to either an increased

production or diminished absorption of cerebrospinal fluid As there was clearly an excess of fluid he suggested the name of otitic hydrocephalus which seems in my opinion a very adequate description

Arachnoiditis

Arachnoiditis[13] inflammation of the arachnoid causing thickening and adhesions often associated with cystic collection of cerebrospinal fluid is sometimes found in the posterior fossa and may simulate abscess formation This condition has been described also under the title of circumscribed serous meningitis Chronic infection in the ear and petrous bone is the usual cause of this condition but it also occurs in connection with acute infections

Otitic Abscess

Otitic abscess may occur by whatever pathway arising either in the tempero sphenoidal lobe or in the cerebellum and more often in the former than in the latter The following table gives examples —

Author	*Number of Cases*	*Temporal*	*Cerebellar*	*Elsewhere*
Oppenheim	76	55	13	8
St Bartholomew's Hospital London	48	6		—
Evans	109	6	40	–
Atkinson	1	1	9	—

The path of infection in cases of abscess in the *temporal lobe* usually is via the tegmen tympani or roof of the attic whilst infection of the labyrinth and lateral sinus usually leads to cerebellar location The middle third of the temporal lobe is the usual area involved whilst the anterior and outer part of the lateral cerebellar hemisphere commonly is involved in subtentorial abscess formation The abscess is almost invariably on the side of the affected ear but cases have been recorded in which a contralateral abscess has occurred In such a case the infection must have been carried by the blood stream Brain abscess may be acute or chronic, the determining factors being no doubt time and the virulence of the infecting organism The abscess may be entirely sub

cortical, but frequently pus is found immediately below the cortex or quite superficially The site of the abscess is likely to have an important effect on the condition of the cerebrospinal fluid, as in the more deeply situated type there may be little or no meningeal reaction unless there



FIG 1 —Case of acute brain abscess opened by operation The abscess has ruptured into the anterior horn of the right lateral ventricle Note softening of cerebral tissue in neighborhood of abscess with hemorrhages and lateral ventricles filled with blood and pus.

is a co existing leptomeningitis In cases of chronic abscess there may be a thick fibrous capsule This in long standing cases may actually show evidence of calcification In the acute variety no capsule can be identified the area surrounding the pus being more or less diffluent with punctate hemorrhages and thromboses of small vessels

Infection from the *nose*, commonly from the frontal sinus acts in a similar manner to infection from the ear and may cause an extradural abscess leptomeningitis or an abscess in the frontal lobe In this case too the abscess is likely to be single, acute or chronic

Metastatic Abscesses

Metastatic abscesses almost invariably are acute A good account of these has been given by Joseph L J King[18] Like other acute brain abscesses they are found to consist of a central purulent core surrounded by a zone of necrotic tissue, outside which is a ring of encephalitis The great danger in such cases, which is not as a rule long delayed is intraventricular rupture

Morbid Anatomy

The appearances presented by a brain abscess on examination after death depend on the chronicity or otherwise of the abscess In the acute cases there is no definite wall to the abscess cavity simply a ragged margin formed by more or less completely softened and edematous cerebral tissue In these circumstances the contents of the abscess are apt to consist of a thin pinkish material formed as the result of breaking down cerebral tissue with the addition of a certain amount of blood and pus (Fig 1)

In the more chronic cases there may be and usually is a very definite wall to the abscess cavity the thickness of which varies with the chronicity of the abscess (Fig) This wall is formed of loose fibrous tissue in connection with which there is a cellular infiltration in which numbers of plasma cells are usually to be noted

The contents of the abscess cavity often are very characteristic greenish yellow or actually green in color and often very offensive In a number of chronic cases the pus on culture has proved sterile There is often an extradural collection of pus in abscess formation secondary to suppuration in connection with the ear or cranial sinuses though it is to be noted that such a collection of pus may exist alone without the occurrence of any cerebral infection

In the event of an abscess being unrelieved by operation its eventual termination is by rupture either internally into the lateral ventricle or externally on the surface of the brain In both cases septic meningitis results and death speedily follows Very occasionally a cerebral abscess may discharge its contents through the ear a purulent otorrhea being set up If for any reason the escape of pus becomes restricted cerebral symptoms quickly follow owing to the increase in the intracranial pressure that immediately follows

Cerebrospinal Fluid

This should of course form part of the routine neurological examination of the patient but the results of the examination of the fluid are very variable The possible significance of the findings must be weighed very carefully with the clinical evidence The findings are complicated by the presence or absence of frank leptomeningitis



Fig 2—Case of chronic abscess of brain in temporosphenoidal lobe Note thick wall of abscess and absence of inflammatory reaction in surrounding cerebral tissue

Usually, but by no means constantly, *pressure of the fluid* is raised Of 12 cases personally observed the pressure was not raised above 120 mm in 5, was between 150 mm and 200 mm in 5 and was between 200 mm and 300 mm in 2 A manometer usually is available for measuring the pressure accurately but in its absence two drops per second represents a pressure of about 150 mm

In 24 cases of proved abscess the fluid was clear in 15, turbid or cloudy in 7 and purluent in 2

Estimated in 22 cases spinal fluid *protein* was stated to be normal (20 to 40 mgm) in 3 cases, 40 to 70 mgm in 6 cases 70 to 100 mgm in 5 cases and over 100 mgm in 8 cases, from which figures it is clear that some rise is the rule and that this may be considerable

Usually the *cellular contents* shows some increase numerically but there may be none The number of cells may vary in cases of uncomplicated abscess Quite high cell counts may occur without definite leptomeningitis being present and in such cases the fluid is likely to prove sterile on culture and the cells to diminish in number with repeated lumbar puncture in event to which Borries has applied the term paradoxical benignancy In 21 cases of proved abscess the

following cell counts were found, 3 cases 5 to o cells per cu mm 3 cases 50 to 100 cells . cases 100 to oo cells 4 cases 200 to 500 cells cases 500 to 750 cells, 1 case 750 to 1 000 cells In some of the higher counts there was evidence of acute leptomeningitis

With a deep seated abscess uncomplicated by meningitis there may be no increase in cells or protein in the fluid When the abscess is situated nearer the cortex there is likely to be either a lymphocytic or polymorphonuclear reaction in the meninges, whilst with frank meningitis the cells will be polymorphonuclear In the series of cases referred to polymorphonuclears were present in 19 of the 2. cases and in excess in 9 cases Lymphocytes were in excess in 11 cases, and in 1 case there were equal numbers of each

The *chlorides* in the fluid tend to fall with the development of leptomeningitis so the estimation of the chloride content of the fluid may be very helpful in diagnosis A definite fall below 700 mgm per 100 c c of spinal fluid with an increased quantity of protein and a high cell count is very suggestive of meningitis The lower the chloride count the more suggestive it becomes I have records of a case in which a temporal abscess existed in which there were 1 000 cells per cu mm in the fluid with a chloride content of 730 mgm per 100 c c Culture of the fluid was sterile and there was no generalized meningitis

The *glucose content* of the fluid is unaltered with uncomplicated abscess and definite reduction in quantity only occurs in the presence of meningitis

Symptomatology

The early symptoms of brain abscess are those of the condition which gives rise to it Acute or chronic infection of the ear or nose suppurative conditions in the lungs septicaemia or pyaemia these will give rise to fever tachycardia anorexia and headache as general symptoms if the condition is acute or there may exist chronic otorrhoea or a chronic infection of frontal sinus or lung which will cause their own appropriate symptoms When to these are added signs of increasing intracranial pressure anxiety as to the possibility of intracranial complications will of course arise Symptoms in cases of uncomplicated brain abscess are general and local

General Symptoms

For a time there may be a latent period particularly in otitic cases during which there is little noticeable change in the patient. As the abscess develops there is likely to be an obvious change in personality. The patient may become irritable and mentally retarded. Lack of attention is combined with listlessness or apathy. Questions will be answered possibly correctly after a more or less prolonged latent period. Headache is likely to be a prominent symptom, often a continuous dull ache with paroxysms of violent pain. This may be experienced on the affected side and there may be tenderness on percussing the bone in the area complained of. The tongue becomes dry and coated and the breath offensive. Vomiting is likely to occur. The bowels are constipated. The temperature chart varies considerably, even in uncomplicated brain abscess; irregular pyrexia or a normal or subnormal temperature with occasional peaks of slight pyrexia all occur. Never, if one is justified in using such a term in medicine, is the temperature continuously high. Of course acute cases of ear or nasal infection, acute pulmonary conditions and so on will cause fever, as will also other intracranial complications if these be present, such as meningitis or lateral sinus thrombosis. Rigors probably will occur with the latter.

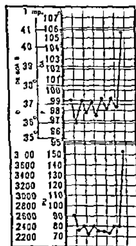


Fig 3.—H A G aet 45. Influenza 14 days before admission. Right sided subcortical abscess which ruptured into lateral ventricle. Note sudden rise in temperature and frequency of pulse.

Should an abscess rupture into the lateral ventricle there is likely to be an abrupt rise in temperature and pulse rate as illustrated in the accompanying chart (Fig 3). In such a case pure pus will be found in cerebrospinal fluid. Rupture, however, may occur without such dramatic rise in temperature.

The pulse rate in uncomplicated cases seldom is accelerated and may indeed be definitely slowed. With rapidly rising intracranial pressure this slowing may be very marked although perhaps not continuously. Unless frequent observations are made, every hour or half hour, the fall in pulse rate to 50 or even 40 per minute may escape observation.

In the late stages of brain abscess with greatly increased intracranial pressure the respiratory rhythm usually changes with the development of the Cheyne-Stokes type. If unrelieved the patient may die from

respiratory failure, such an occurrence being more common in abscess below the tentorium than elsewhere. Papilloedema is met with less commonly than in tumours of the brain and as with the latter at first may be unilateral. This as in tumour cases may be suggestive as to the side on which the abscess is located but is by no means invariably homolateral. Short of papilloedema the retinal veins may be obviously congested with slight blurring of the disc margins.

Examination of the blood rarely is characteristic although there is usually a slight increase in white cells from 10 000 to 1 000 per cu mm, the differential count showing an increase in polymorphonuclear cells.

Local Symptoms and Signs

Local signs and symptoms will depend on the situation of the abscess: frontal lobe in cases of nasal infection, temporal or cerebellar in otitic cases, usually centrum ovale in cases of metastatic abscess and anywhere in traumatic cases. The signs of a local space occupying lesion are identical with those caused by a brain tumour but as with the latter there may be for a long time no definite symptom or sign of localising value. Under such circumstances the general signs and symptoms are therefore the most important indications for further investigation in the form of exploratory operation.

I do not propose here to give a detailed description of the symptoms and signs which may occur as the result of local disease in different areas of the brain. The reader is referred for a description of these to the appropriate chapters in this system. I think however it is worth referring briefly to the symptoms which I have found the most helpful in localisation.

Temporal Lobe Abscess.—Aphasia occurs when the abscess is left sided in a right handed individual or is right sided in a left handed individual. The type of aphasia in such cases is very characteristic. It is known as nominal aphasia, the patient being unable to find the correct word for an object which he can recognize perfectly well and the use of which he can indicate by pantomime. He will recognize the name correctly when it is given him. When this symptom is only present in an early stage it may be necessary to carry out an extensive investigation before evidence of some degree of nominal aphasia is found but it is in my opinion the most common and most important sign locating the abscess in the temporal lobe.

The next most common sign in such cases is weakness of the face on the opposite side to the abscess This weakness is of the supranuclear type and must not be confused with a possible peripheral type of facial weakness on the homolateral side due to involvement of the facial nerve in the petrous bone Weakness or absence of the abdominal reflexes on the contralateral side also is important

A lesion in the temporal lobe extending inwards is likely to disturb the optic radiations and to produce a partial homonymous hemianopia The characteristic visual field under these circumstances is one in which there is a quadrantic defect usually in the superior quadrant, but in cases of abscess by the time this sign may have developed, the patient is more often than not unable to cooperate sufficiently to make the test of any value

Cerebellar Abscess—It is important to note that in a large proportion of cases there are no definite cerebellar signs present Nystagmus, when due to a cerebellar lesion usually shows a coarse movement towards the side of the lesion and a fine movement towards the opposite side There are however other possible causes of nystagmus to be found in the damaged ear itself e g infection of the labyrinth, so that the significance of the symptom has to be weighed very carefully in any particular case The type of nystagmus usually is horizontal and arrhythmic when present in cases of cerebellar abscess whilst in labyrinthine infection there is a greater probability of a rotary element in it There are two points which may help to differentiate between labyrinthine and cerebellar nystagmus, namely that in the former the movement is more likely to have a rotatory element and to be finer and also that the nystagmus may be affected by changing the position of the head

Frontal Lobe Abscess—There may be no evidence of a focal character in these cases and only general symptoms suggesting abscess formation may occur The presence of a grasp reflex or an absent abdominal reflex on the opposite side if present will be very suggestive Localized tenderness on percussion of the bone is not of much value here as this will occur in any case with sinus infection

Metastatic Brain Abscess—As these cases are embolic in origin the onset in most, as might be expected is sudden and acute Severe pain in the head dizziness and vomiting accompanied by a rise in temperature occurring in a patient with chronic pulmonary suppuration or pyaemia is only too suggestive of cerebral metastasis within a day or two hemiplegic symptoms are likely to supervene The pulse rate at first at any rate is likely to be raised It may or may not fall with the

progress of the abscess On the other hand the onset in the chronic cases may be quite insidious although the signs, albeit slowly develop ing are ultimately those of a space occupying lesion The situation of these metastatic abscesses is most commonly in the centrum ovale

Prognosis in these cases is very serious Untreated the average dura tion of life in the acute cases was found by Schorstein to be 10 days from the onset of cerebral symptoms The immediate cause of death is often rupture into a lateral ventricle followed by a rapidly fatal meningitis

In Schorstein s paper[8] published in 1909 there had never been any recovery recorded in the case of a metastatic brain abscess Hurst[18] in 19 5 recorded a case successfully treated by operation probably a chronic abscess occurring in a patient with an empyema Joseph King[16] has published an excellent review of the subject when reporting 6 cases on which he operated with recovery in one acute abscess and mentions Roulland[19] in 1917 as reporting the first recovery of an acute metastatic abscess treated by operation King[16] stresses the importance of early operation in these cases probably not later than the sixth or seventh day and emphasizes the danger of rupture into the lateral ventricle being precipitated by operation

It seems certain I think that the improved technique in treating chronic pulmonary suppuration and the advent of penicillin and the sulfonamide group of drugs should reduce the incidence of metastatic brain abscess very materially

Diagnosis

The diagnosis of brain abscess may be comparatively easy or on the other hand one of the most difficult problems in medicine Where a chronic suppurative otitis media exists and the patient develops the symptoms already detailed with localising signs of a focal lesion in temporal lobe or cerebellum the diagnosis is reasonably obvious Great difficulty exists in the acute cases for in them a variety of intracranial complications may occur and either mask or simulate the presence of a brain abscess such complications include meningitis extradural abscess perisinus abscess, lateral sinus thrombosis circumscribed serous menin-gitis, otitic hydrocephalus acute nonsuppurative encephalitis very rarely diffuse subdural suppuration and what has been termed Gradenigo s syndrome In addition to this local disease in the inner ear such

as acute labyrinthitis may suggest the presence of a cerebellar lesion

With regard to the differential diagnosis of these several conditions meningitis is established by examination of the cerebrospinal fluid and by pyrexia, nuchal rigidity and so on but may be associated with brain abscess Should symptoms suggestive of the latter persist with improvement of meningitis by appropriate therapy, the probability of abscess is much enhanced

Extradural and perisinus abscess produce no diagnostic points peculiar to themselves but are likely to be discovered, when the general condition indicates operative treatment, as it will certainly do Lateral sinus thrombosis too, although it may be on occasion without obvious symptomatology usually reveals itself by rigors, sweats swinging temperature and rapid pulse symptoms at marked variance with those of brain abscess Headache and mental hebetude are not prominent while vomiting and papilloedema are most unusual Acute non suppurative encephalitis and diffuse subdural suppuration are undiagnosable till the condition is revealed at operation

Circumscribed serous meningitis as it leads to increased intracranial pressure particularly in the posterior fossa, may simulate a cerebellar abscess but the absence of mental hebetude and the normal or near normal condition of the cerebrospinal fluid makes the presence of abscess doubtful No doubt operation will be indicated, when the gush of clear fluid on opening the cyst establishes the diagnosis

Otitic hydrocephalus with its symptoms of severe headache, papilloedema and often sixth nerve palsy at first sight may appear deceptive It is clearly differentiated by the mental alertness of the patient, absence of pyrexia and by the normal character and greatly increased quantity of cerebrospinal fluid As already pointed out the fluid may be under very great pressure

Gradenego s syndrome is the name given to a complication of mastoiditis which consists of severe headache on the side of the affected ear, with sixth nerve palsy on the same side, the latter probably due to a toxic neuritis of the sixth nerve as it crosses the apex of the petrous bone where mastoid air cells extend far down that bone It is clear that in these cases of acute otitis with evidence of intracranial extension a firm diagnosis of abscess often cannot be made with precision However as in most of these cases exploratory operation is indicated the evidence of abscess formation is likely to be forthcoming a remark which applies equally to frontal sinus suppuration

Traumatic Brain Abscess

In many of these the diagnosis is difficult or impossible, and for the following reasons in wounds of the head of which we have seen so many examples in the last few years septic meningitis frequently complicates the picture, or the abscess may remain latent until rupture and the development of meningitis reveal its presence or on the other hand, cerebritis with edema but without the formation of pus may lead to a mistaken diagnosis of abscess

If meningitis of the convexity of the brain follows an injury in that locality one may meet with headache vomiting fever combined with mental changes, such as dullness and drowsiness deepening perhaps to coma Should this be accompanied by monoplegia or focal convulsions considerable doubt will exist as to whether an abscess has been formed or not Evidence of meningitis in the cerebrospinal fluid does not exclude the possibility of an abscess being present nor should its presence contra indicate operation

If such symptoms as just referred to develop insidiously a week or more after an injury show a tendency to remission and are accompanied by the development of papilloedema one can surmise that an abscess is developing Focal epilepsy or paralysis is more in favor of abscess formation than meningitis alone but both may occur as the result of cerebritis unassociated with abscess formation as may also an infrequent pulse and comparatively low temperature As an example of such a condition the following case is interesting

J B aet 4 Wounded in right frontal region Operation next day excision of wound small depressed fracture of inner table of skull enlarged dura was thought to be intact September 3 admitted to a London military hospital complaining of severe headache, frontal and occipital Insomnia due to headache drowsy and irritable no vomiting Temperature rose to 100 F as a rule in each twenty four hours often 98 to 99° F Pulse varied from 48 to 60 per minute small and of poor tension.

September 6 Wound opened up and B I P P applied, no improvement in general condition

September 10 Still in same condition but (1) pulsation in wound over forehead has ceased ( ) has choked discs with blurred edges and congested veins (3) no positive signs in examination of nervous system Lumbar puncture was performed and fluid reported normal

September 14 Operation performed, wound enlarged Dura found thickened and adherent over right frontal lobe Increased tension present Brain explored by puncture but no pus found

September 21 Temperature now normal, pulse rate 60 to 72, very irritable and negative in mental attitude

October 3 Very well, no headache, normal temperature and pulse

In this case the symptoms were clearly due to the presence of a brain lesion compatible with abscess, but the sequel showed that none was present, cerebral edema due to cerebritis having simulated the symptoms of an abscess

As an example of a latent brain abscess of traumatic origin which was unsuspected I will briefly refer to the following case

R R wounded August 9th, 1918, fractured vertex with in driven bone fragments Operation next day with excision of wound and removal of fragments

Left hemiplegia followed the injury at once

Condition on October 29 1918 on admission to a London military hospital, temperature, pulse respiration normal Seven and one half inches from nasion there is a cerebral hernia, partially bridged over by skin Anteroposterior diameter of hernia, two inches Hernia not raised particularly nor very tense Left hemiplegia and hemianesthesia, optic discs negative

November 8 Condition improving, hernia getting smaller

November 13 Woke screaming with pain in head, then became dull and lethargic, no rise in temperature, pulse 112 per minute Cerebrospinal fluid found thick and turbid, due to streptococcal meningitis

Died fourteen days later Meningitis caused by rupture of brain abscess into the ventricle

In some cases a considerable period has elapsed between the injury and the development of symptoms due to abscess formation

In a case under my care at the National Hospital Queen s Square, London, the patient was wounded in September, 1918 in the left occipital region In May, 1919 he developed fits of general epileptic character In April, 19 0 he complained of severe occipital headaches (eighteen months after his original injury), papilloedema developed in both eyes and an abscess was discovered in the left occipital lobe How long the abscess had been present in a latent condition is problematical, but it is not unreasonable to suppose that it had existed for some months

Primary Brain Abscess

It is very doubtful if such a condition as primary brain abscess ever occurs It is however true enough that cerebral abscesses are found at operation or in the post mortem room which have been quite unexpected and for which there is nothing either in the clinical history or physical examination to suggest what might have been the origin of the infection It is a matter of great importance to get a really accurate clinical history Whilst this is true for any case of disease it is particularly important in connection with cases of intracranial disease It is very easy for the patient to forget an earache, a cold in the head and so on unless his attention is particularly directed to such possibilities and the original occurrence may have been quite trivial and so the more easily forgotten yet in all probability the seeds of intracranial trouble were sown during this apparently trivial and forgotten infection

In the absence of any obvious cause for abscess formation in the brain the possibility that such a condition may exist is likely to be discarded in favor of the more probable existence of a new growth Lumbar puncture and examination of the cerebrospinal fluid might enable an accurate diagnosis to be made

The following case illustrates very well several points in connection with uncomplicated brain abscess apparently primary in origin

T N aet 4 came under observation on May 29 1918 giving the following history

Since January a change had been noted in his disposition He had become irritable depressed and absent minded There was no history of any preceding illness In March his eyesight began to fail On May 10 he had complained of frontal headache and had an attack of dyspnea May 11 he complained of weakness in the legs more particularly the left leg May 15 he vomited twice and since then had suffered from constant frontal headaches For the week before his admission he had not spontaneously taken any food and had had to be fed He had been confused mentally did not know the days of the week and so on

On examination his memory was found to be defective and his powers of attention and cerebration generally below normal The sense of smell was impaired on the right side There was papilloedema in the right eye but not in the left He was incontinent his gait was unsteady, the reflexes were natural

June 8 Pulse rate had fallen to 64 per minute he was stuporose the left plantar reflex was now extensor June 11 Operation Bone re

moved over right frontal parietal region, dura tense, not opened After the operation the general condition improved June 16 Further operation Dura opened Convolution found flattened, no meningitis The cortex was incised and pus evacuated The patient went downhill after the operation and died

Post mortem an abscess cavity was found in the posterior part of the right frontal lobe, with a fairly definite wall of fibrous tissue No septic focus was found in connection with any of the cranial sinuses, nor in the ears The viscera generally were free from disease

The history and clinical features presented in this case had suggested the pressure of a tumor of the brain, and abscess was not suspected

The Wassermann reaction in blood and cerebrospinal fluid was negative Unfortunately there is no record of chemical or cytological examination of the fluid

Metastatic Brain Abscess

When a patient who is suffering from bronchiectasis lung abscess or pyaemia from whatever cause arising, develops symptoms pointing to an intracranial complication, the diagnosis, as a rule will lie between meningitis or brain abscess Lumbar puncture and examination of the cerebrospinal fluid will quickly differentiate between these conditions It is true that meningitis may follow the development of a brain abscess but before it does so the presence of the latter usually will have been indicated by the occurrence of severe headaches drowsiness with increasing apathy vomiting and the other symptoms to which reference has already been made

Brain Abscess due to Extension from a Focus of Infection in the Skull

The chief sources of such extension as has been mentioned already are the frontal ethmoid or sphenoidal sinuses and otitic infection Spread of infection from the frontal or ethmoidal sinuses is more likely to cause a brain abscess than a similar occurrence in connection with the sphenoidal sinus in which case meningitis or cavernous sinus thrombosis is the more probable result There may be no localising signs whatever in a case of frontal lobe abscess and the diagnosis must be made from

general symptoms, combined with a careful examination of the posterior wall of the frontal sinus at operation. Should the patient's condition not improve following operation on the sinus the brain should be explored by puncture. Thickening of the dura behind the sinus is a very suggestive indication of the brain abscess.

Treatment and Prognosis

As is so often the case prevention is better than cure. With the recent developments in the treatment of infections by penicillin and the sulfonamide group of drugs and the advances made by surgery in dealing with chronic pulmonary sepsis there are good grounds for belief that the incidence of brain abscess will be reduced.

The improvement in the technique of brain surgery holds out prospects of more favourable results when a brain abscess has developed. King has shown that even in metastatic abscess once invariably fatal some success has been obtained. At present the results of surgery have never reached MacEwen's figures published towards the end of last century in which he was able to record 18 cures in 19 cases. The explanation for his remarkable success is no doubt that all his operations were done on carefully selected and chronic cases where a definite capsule had formed but the possibility of success in acute cases precludes such waiting tactics at the present time.

BIBLIOGRAPHY

1. MACEWEN, W M. Pyogenic Infective Disease of Brain and Spinal Cord. Macmillan, New York, 1893.
2. EVANS, W. The pathology and aetiology of brain abscess. Lancet, 1931, I, 1231 and 1289.
3. RUEGG, C. Beitrag zur Frage uber Haufigkeit und Vorkommen otitischer Hirnkomplikationen. Inaugural Dissertation, 38 pp. Basel, 1927.
4. TURNER, A L and REYNOLDS, F E. Intracranial Pyogenic Diseases. Oliver and Boyd, Edinburgh, 1931.
5. WILSON, S A K. Neurology, edited by A N Bruce. Arnold, London, 1940.
6. SHORSTEIN, G I. Lecture on abscess of the brain in association with pulmonary disease. Lancet, 1909, II, 843.

7 ATKINSON, E M Abscess of the Brain its Pathology, Diagnosis and Treatment Medical Publications Ltd London 1934
8 SYMONDS C P Some points in the diagnosis and localization of cerebral abscess Proceed Royal Soc Med, 19 7 XX Pt III 1139 Some points in the diagnosis and localization of brain abscess Jour Laryngol and Otology, 19-7 XLII, 440 Otitic hydrocephalus Brain 1931 LIV, 55
9 ADSON A W Pseudo brain abscess, Surg Clinic North America 19 4 IV 503
10 BORRIES, G V TH L Encephalite otogene hemorragique, Rev de Laryngol Otol et Rhinol 193 LIII, 49
11 TAYLOR F Manual of the Practice of Medicine 1st ed p 26 Churchill London 1890
1 QUINCKE H Ueber Meningitis serosa und verwandte Zustand Deutsch Zeitschr f Nervenheilk 1897 IX 149
13 WARRINGTON W B Intracranial serous effusions of inflammatory origin meningitis or ependymitis serosa meningism—with a note on peudo tumours of the brain Quart Jour Med 1914 VII 93
14 PASSOT R Meningites et etats meninges aseptiques d origine otique, These de Paris 99 pp G Steinheil Paris 1913
15 HINDS HOWELL C M Arachnoiditis (president s address) Proceed Royal Soc Med 1936 XXX (Sect Neurol) 33
16 KING J E J Acute metastatic brain abscess, Southern Surgeon 1936 V 407
17 EAGLETON W P Brain Abscess Macmillan New York 19 2
18 HURST A F A case of cerebral abscess complicating empyema operation and recovery Lancet 19 5 I 605
19 ROULLAND H Abces metastatique du cerveau au cours d une suppuration pleurale Trepanation drainage de l abces guerison Paris Chir 1917 IX, 613

September 1 1948

CHAPTER V

CRANIO-CEREBRAL INJURIES

By DONALD MUNRO

By DONALD MUNRO

TABLE OF CONTENTS

INTRODUCTION

Although the treatment of cranio cerebral injuries belongs in the last analysis in the field of surgery the prevalence of these lesions makes it imperative that every practising physician be familiar not only with the physio pathology involved but with the diagnosis the general principles of treatment and the maximum permissible morbidity and mortality that should accompany each individual type of injury With this knowledge the physician is able to deal competently with the emergencies he will recognize the need for surgical or special consultants at the earliest possible moment and will know whether or not the surgery that is being practised on his patient is proper and in conformity with the pathological

requirements and of a type that can be expected to give the patient his best chances for recovery without morbidity This does not and should not in a text book on medicine imply any discussion of the purely technical aspects of any operative procedure The physician must leave that to the surgical consultant whose knowledge and efficiency are tested by the results he obtains and not by carping criticism of meticulous details of technical procedure On that account this section will be devoted largely to a discussion of the non surgical aspects of cranio cerebral injuries Other information must be sought for if desired from other sources references to which are listed at the end of the section

Physio pathology of Cranio cerebral Injuries

Cerebrospinal Fluid

Anatomy — The cerebrospinal fluid in all probability is a dialysate, which has been filtered from the blood stream into the ventricular system of the brain by the choroid plexus It leaves the ventricular system through the foramen of Magendie in the roof of the 4th ventricle to be distributed throughout the cranial and spinal subarachnoid spaces At certain points in relation to the brain stem and the base of the brain the subarachnoid space is dilated locally The dilatations are spoken of as cisternæ or cisterns and the cerebrospinal fluid puddles in them The best known of these cisternæ is the cisterna magna which surrounds the junction of the cervical spinal cord with the medulla and which lies just beneath and on either side of the rim of the foramen magnum It is at this site that the cisternal puncture as devised by Ayer is made It is well to emphasize here that this cisternal puncture is never required for either the diagnosis or the treatment of any cranio cerebral injury and if used under such circumstances is an extremely dangerous procedure Other cisternæ are the lateral cerebellar the pontine the chiasmal and so forth The rest of the subarachnoid space overlies the cerebral cerebellar and spinal pia with its enclosed vessels and immediately underlies the cranial and spinal arachnoid It is broken up by innumerable filmy trabeculæ and is crossed at intervals by veins which have originated as branches of the pial veins and are on their way to empty into dural veins or into some one of the large dural venous sinuses Such vessels usually are referred to as bridging veins From the time they leave their parent pial vein until they reach their destination in the dura their walls are entirely without support and their ability to lengthen without rupture at a minimum The cerebral subarachnoid space is characterized further by the presence

of arachnoidal villi or Pacchionian bodies These structures are out pouchings of the arachnoidal membrane into the venous blood stream Thus the subarachnoid space is not actually in contact with the blood stream but is separated from it by the greatly attenuated dural wall of the sinus and the arachnoid itself This intervening wall is perforated by many small openings These are less than the diameter of a red blood corpuscle and therefore permit the movement of fluid but not of cells from one side to the other It is through these structures that the cerebro spinal fluid is absorbed into the cranial venous system

Cerebrospinal Fluid Circulation — The cerebrospinal fluid is being constantly produced at all times It fills the ventricles the cisternæ and the spinal cerebellar and cerebral subarachnoid spaces To do this it must be manufactured at a positive pressure Only in this way can these various cavities be kept in a state of normal distention However to prevent over-distention and in view of the constant replenishment of the supply provision must be made whereby the excess fluid can be removed as constantly as formed This as pointed out above takes place via the arachnoidal villi into the cranial venous blood stream and is possible only because the normal cerebrospinal fluid pressure is slightly greater than the normal intracranial venous pressure It will be apparent that in such a mechanism the two pressure levels must be interdependent and altera tions in either one must affect directly and at once the height of the other Thus while under normal conditions the flow of cerebro spinal fluid will be constantly out of the ventricles into the subarachnoid space and thence into the cranial venous system a wide variety of abnormalities may be expected to reduce this movement to any degree and even to stop the stream completely

Cerebrospinal Fluid Pressure — The normal cerebrospinal fluid pressure has been known for a long time It varies with the position and size of the patient The standard measurements are those for adults lying com pletely relaxed on either side and with the head level with the pelvis These measurements are commonly made by tapping the lumbar sub arachnoid space Under these conditions the normal cerebrospinal fluid pressure is known to lie between 8 and 10 mm of mercury and 90 and 160 mm of water Figures slightly above or below these limits may be normal in the individual case The amount of dehydration the size of the individual the efficiency of his circulatory system and especially the degree of relaxation are all factors which may or may not be recognizable but which can produce variations from the figures given above The measurements in the new born have been made only on the mercury scale This normal pressure ranges from 2 to 5 millimeters of mercury It is not

known when the change to adult levels takes place nor how gradual it is Measurements used with the patient in the erect position and at the same point show that in an adult the lumbar pressure will be more than doubled The intracranial pressure on the other hand will be less than atmospheric and range from minus 50 mm in the ventricles to 150 mm in the lumbar sac while the zero point between these two extremes will be found to be at about the level of the lower cervical vertebræ Analogous measurements have not been made on the new born Changes in cerebrospinal fluid pressure which for practical purposes is the same thing as intracranial pressure follow any alteration in the volume of any of the contents of the skull This except in unimportant details was first stated in 1824 as the Monro Kellie doctrine and predicates that variations in any one of the three elements within the cranium viz brain blood or cerebrospinal fluid may occur but any alteration in the volume of any one is compensated for at once by an alteration in one or both of the others Thus it will be seen that if the brain volume is increased as in œdema the amount of cerebrospinal fluid may be reduced and the size of its reservoir curtailed So too with an increase in the volume of intracranial blood as for example in congestion associated with anoxemia the same thing may happen In either case the cerebrospinal fluid or intracranial pressure rises inasmuch as the production of the spinal fluid continues in the face of the reduction of the reservoir Conversely when the brain shrinks as in dehydration the cerebrospinal fluid reservoir is enlarged and until the extra intracranial space that has been produced in this way is again distended by fluid the intracranial pressure will be below normal

Cerebral Circulation

Arterial —Arterial blood is brought to the brain by four main arteries the two vertebral and the two internal carotid arteries and is distributed evenly from them to all six cerebral trunks Thus an adequate supply of arterial blood is insured to both hemispheres even if one carotid be shut off The branches from the six main trunks divide in such a way as to supply the basal ganglia the choroid plexus and some of the deep white matter Most of them however run directly to the surface of the cortex where they spread out in the pia From these vessels arterioles perforate the surface of the brain and plunge directly downward into the cortex and subcortical white matter At these levels they branch again and again and eventually enter the capillary bed These arterioles and capillaries have a rich anastomosis with branches from other arterial trunks including those that have ascended from the vessels that have

come up through the basal ganglia and white matter There are no end arteries in the brain All of these vessels however and especially the arterioles are under the control of the vasomotor apparatus although to a lesser degree than the other parts of the arterial tree As a result they may either dilate or go into spasm as the result of impulses that arise outside of the cranial cavity

Capillary Circulation — The capillary network is much more dense in the gray than it is in the white matter and also has a rich anastomosis Blood flow in any given capillary loop is directly dependent upon the degree of contraction of the arteriole that leads to that loop Under normal conditions the resulting intracapillary pressure at the arterial end of the loop is kept constantly at a slightly higher level than the osmotic pressure of the tissue fluid which surrounds the loop These pressures being antagonistic the higher hydrostatic pressure insures movement of oxygen laden nutrient fluid outward into the perivascular and thence into the pericellular spaces At the venous or opposite end of the same loop the hydrostatic pressure inside the vessel is less than the colloid osmotic pressure As a result the movement of fluid will be out of the pericellular and perivascular spaces across the capillary wall into the lumen of the vessel In this way provision is made for the removal of oxygen poor tissue fluid from about the cells into the venous circulation It must be evident then that any change such as an increase in the intracapillary pressure or a dilution of the blood plasma will result in the movement of more fluid from the arterial side of the loop into the perivascular spaces as well as an associated diminution of flow of this same fluid from the tissue spaces into the venous end of the loop So too alterations in the protein content of the perivascular fluid will alter the relative osmotic pressure of the blood plasma and the tissue fluid and will of itself alter the amount and absorption of the pericellular fluids

The Perivascular and Pericellular Spaces and Fluid — All of the large and small arteries and veins contained within nervous tissue are enclosed in a well-defined perivascular space This space is not discernable as such about the arterioles venules and capillaries but is present potentially When it is distended it can be shown to be continuous with the perivascular spaces about the larger vessels In the other direction it has been demonstrated that this pericapillary space is continuous with the pericellular or perineuronal spaces In conformity with this arrangement it has been found that the capillaries are in close approximation to the individual nerve cells Furthermore they are more numerous in the cellular as opposed to the axonal layers of the brain the ratio being about 5 to 1 Although it has not proved practical to collect or analyze it the peri

cellular spaces undoubtedly contain extracellular tissue fluid This fluid originates from the blood plasma and passes from the pericellular into the pericapillary and perivascular spaces From this point the flow continues toward the surface of the brain where the fluid empties into the subarachnoid space The drainage takes place through a perforation in the pia which is primarily present to admit a blood vessel It is restricted to a minimum because of a ring of inelastic fibrous tissue which surrounds the vessel like a collar This restriction not only prevents excess drainage of tissue fluid but also the regurgitation of cerebrospinal fluid from the subarachnoid space into the subsurface regions Pericellular fluid normally has a lower concentrate of protein molecules than blood plasma Being separated by a dialyzing membrane the capillary wall and being subject to the law of osmosis it will follow that if otherwise uninfluenced there will be a constant flow of the fluid with the lower molecular concentration toward the fluid with the high molecular concentration These relative osmotic pressures therefore tend to move fluid into the capillary loop from the tissue spaces As was noted above this movement is held in check by the antagonistic hydrostatic pressure within the arterial end of the capillary loop and facilitated by the lowering of that same pressure in the venous end of the loop An abnormal decrease in the molecular concentration or protein content of the plasma or a corresponding increase in the same contents of the tissue fluid may so alter the relative osmotic pressures as to produce not only an excessive outpouring of the former from the arterial end but a diminution of the absorption of the latter into the venous end

Venous Circulation — The venous blood after leaving the capillary bed passes into the large dural sinuses by way of intervening venules and small veins These vessels are more numerous and have more anastomoses than the arteries They are roughly divided into two systems One system drains the ventricles the choroid plexus and the basal ganglia and empties into the vein of Galen by way of the internal cerebral veins This blood leaves the skull through the straight and lateral sinuses to empty into the jugular bulbs The other system drains the subcortical and cortical tissues into vessels that lie enmeshed in the pia on the surface of the hemispheres These empty into the large dural sinuses chiefly the two lateral and the sagittal the blood again leaving the skull by way of the jugular bulbs It is from this group of veins that the bridging vein referred to above arises Mixed with the venous blood after it reaches the sinuses is the excess cerebrospinal fluid which has escaped from the subarachnoid space by way of the arachnoidal villi as described above Cranial venous blood circulates at a positive pressure which is normally

slightly less than that of the cerebrospinal fluid The entire venous system reacts rapidly to any interference with the flow in any part and the intravenous pressure is sufficiently low in the intracortical part of the system at any rate to offer little resistance to extraneous compression such as that exerted by tissue edema Congestion quickly develops and it is but a short step from there to stasis and thrombosis or rupture or both It is because of the widespread and often unexpectedly lethal effect of congestion on the cerebral cells that compression of the jugulars in doing the Queckenstedt test in the presence of cerebral injury is contraindicated It adds more congestion to an already over-distended cranial venous system and may be reasonably expected to rupture veins that might not otherwise break

The Fundamental Pathology

There are certain pathological changes which are constant in all craniocerebral injuries that have been accompanied by any degree of unconsciousness They produce alterations in the normal activities of the cerebral circulation the volume of the brain and the absorption of the cerebrospinal fluid These are demonstrable clinically as changes in the cerebrospinal fluid or intracranial pressure and the presence or absence of blood in the subarachnoid space They constitute the pathology of all the nonoperable cerebral injuries It is to this pathology that the changes associated with the operable cranio-cerebral injuries and the complications that may be associated with either group are added An understanding of and familiarity with this fundamental pathology and the diagnostic and therapeutic requirements that arise out of it are indispensable if one would assume the responsibility for the welfare of patients with craniocerebral injuries

The Vaso vagal Reflex —When an individual is struck on the head sufficiently hard to produce any degree of unconsciousness a reflex dilation of the cerebral arterioles is produced This is the vaso vagal reflex It may arise as the result of many extra cerebral stimuli of which pain and fright are two important ones The stimulus travels by way of the vagus and vasodilator nerves and affects the heart and the arterial side of the circulatory system It produces sweating pallor a lowered blood pressure a cessation or diminution of respirations and a dilatation of the arterioles with a resultant rise in the intracapillary hydrostatic pressure This rise follows the throwing open of the capillaries to the large volume of circulating blood previously held in check by normal arteriolar contractility If the injury has been such or the patient s circulation is so

cellular spaces undoubtedly contain extracellular tissue fluid. This fluid originates from the blood plasma and passes from the pericellular into the pericapillary and perivascular spaces. From this point the flow continues toward the surface of the brain, where the fluid empties into the subarachnoid space. The drainage takes place through a perforation in the pia, which is primarily present to admit a blood vessel. It is restricted to a minimum because of a ring of inelastic fibrous tissue which surrounds the vessel like a collar. This restriction not only prevents excess drainage of tissue fluid but also the regurgitation of cerebrospinal fluid from the subarachnoid space into the subsurface regions. Pericellular fluid normally has a lower concentrate of protein molecules than blood plasma. Being separated by a dialyzing membrane, the capillary wall, and being subject to the law of osmosis, it will follow that, if otherwise uninfluenced, there will be a constant flow of the fluid with the lower molecular concentration toward the fluid with the high molecular concentration. These relative osmotic pressures, therefore, tend to move fluid into the capillary loop from the tissue spaces. As was noted above, this movement is held in check by the antagonistic hydrostatic pressure within the arterial end of the capillary loop and facilitated by the lowering of that same pressure in the venous end of the loop. An abnormal decrease in the molecular concentration or protein content of the plasma or a corresponding increase in the same contents of the tissue fluid may so alter the relative osmotic pressures as to produce not only an excessive outpouring of the former from the arterial end but a diminution of the absorption of the latter into the venous end.

Venous Circulation. — The venous blood after leaving the capillary bed passes into the large dural sinuses by way of intervening venules and small veins. These vessels are more numerous and have more anastomoses than the arteries. They are roughly divided into two systems. One system drains the ventricles, the choroid plexus and the basal ganglia and empties into the vein of Galen by way of the internal cerebral veins. This blood leaves the skull through the straight and lateral sinuses to empty into the jugular bulbs. The other system drains the subcortical and cortical tissues into vessels that lie enmeshed in the pia on the surface of the hemispheres. These empty into the large dural sinuses, chiefly the two lateral and the sagittal, the blood again leaving the skull by way of the jugular bulbs. It is from this group of veins that the bridging vein referred to above arises. Mixed with the venous blood after it reaches the sinuses is the excess cerebrospinal fluid which has escaped from the subarachnoid space by way of the arachnoidal villi as described above. Cranial venous blood circulates at a positive pressure which is normally

done and since its omission is of no therapeutic consequence and therefore cannot harm the patient it does not seem worthwhile to insist upon its inclusion

When the injury is even more severe it will cause in addition to the concussion and edema and congestion as described above either a contusion or laceration or both of the surface of the brain With either of these conditions one or more of the surface blood vessels will be ruptured the pia torn and blood be emptied into the subarachnoid space Because of their thinner and less elastic walls as well as their numerical preponderance this bleeding is to all intents and purposes from the veins and *not from the arteries It is greater in amount and continues for a longer* time when the veins are congested the amount and length of time varying directly with the amount of congestion Per contra it stops of itself except for the dural sinuses when the congestion and therefore the intravenous pressure is lowered to normal This extravasation of serum and in particular of red blood cells into the cerebrospinal fluid introduces in addition to the edema and congestion a mechanical blockade of the avenues of escape of the cerebrospinal fluid

Thus the already abnormally high intracranial pressure is raised still further by the plugging of the orifices of the arachnoidal villi by these free cells This plugging continues to a varying degree until such time *as the phagocytic meningocytes shall have disposed of the abnormal* subarachnoidal cellular contents In the meantime the cerebrospinal fluid is backed up in its reservoir the cerebral veins and the cerebrum itself *are subjected to the resulting pressure* the congestion tissue anoxia and edema are increased and the cranial venous pressure raised to new heights A vicious circle is produced which can be broken only by the mechanical drainage of the excess backed up cerebrospinal fluid

*It has been said that this therapeutic reduction of the high intra*cranial pressure will promote more bleeding and that therefore it is contraindicated Such a statement has as can be seen no basis in fact and serves *only to betray the ignorance of the author in regard* to the fundamental pathology of the injury with which he has had to deal Such conditions are commonly spoken of as *contusion* and/or *laceration of the brain* In the interests of accuracy and for the purposes of treatment it would be much better for the patients if it were universally recognized by the medical profession that the diagnosis should include *edema and congestion* in addition In this way both dehydration and decompression by drainage of cerebrospinal fluid would be assigned their proper places as therapeutic agents in the *management of the patient*

efficient that recovery of consciousness takes place before the circulatory changes have progressed beyond this point there will be no further symptomatology This will apply not only to the objective demonstration of signs but also to the subjective complaint of symptoms This amount of post traumatic cerebral pathology is self limited, requires no therapeusis and constitutes the syndrome that goes under the diagnosis of *concussion*

If the injury has been more severe or the circulation less efficient the pathological changes will of necessity be greater The period of unconsciousness however need not be affected The changes instituted by the vaso vagal reflex serve now as the first step of more serious and wide spread pathology The dilated arterioles and the increased intracapillary pressure dilate the capillary loop and raise the hydrostatic pressure within it to such levels as to cause an outpouring of plasma from the arterial end into the surrounding perivascular and other spaces These same factors lead to a reversal of the ordinary relationships between the hydrostatic capillary venous pressure and the relative osmotic pressures of the tissue fluids and the venous blood plasma This prevents the absorption by osmosis of the excess tissue fluids into the capillary venous stream The pericapillary tissue spaces distend venules are compressed or collapsed from the pressure of this distention and the circulation in the smaller vessels may be stopped or even reversed A high degree of tissue anoxia follows with swelling and destruction of cells The brain volume increases the cranial venous pressure rises and partly as the result of a diminution of the size of the reservoir and also as the result of diminution of absorption of cerebrospinal fluid from that reservoir into the large venous channels because of the relatively higher venous pressure the cerebrospinal fluid or intracranial pressure is raised Associated with the more serious phases of these changes may be thrombosis or rupture of intracortical veins with areas of hemorrhage or cell destruction that tend to coalesce As a result all varieties and degrees of alteration of peripheral function may follow and remain permanently if the damage has been extensive enough This degree of post traumatic cerebral pathology may be either self limited or progressive If the former the resultant permanent symptomatology will vary with the amount of cellular destruction but in the latter the process will end by causing the death of the individual The therapeusis must of necessity be directed toward the lowering of the increased intracranial pressure the elimination of the venous congestion and the reduction of the increase in brain volume This syndrome goes under the diagnosis of *congestion and edema* or *edema of the brain* The term *concussion* should be added to the diagnosis to make it accurate and complete However custom has decreed that this be not

History

Since generally it is taken for granted that cranio cerebral injuries result from contact between the patient s head and some solid object the most important historical datum that can be obtained has to do with the presence or absence of unconsciousness For practical purposes and because the exceptions to the rule are so rare it may be stated that no cerebral injury occurs without some degree of unconsciousness It is not as easy to verify this statement as would appear on the surface however There is a complete disagreement among the profession and the laity as to what constitutes unconsciousness There is also the ever present desire on the part of the patient to color his story if for no other reason than to please the doctor Furthermore there will be times when the patient is unconscious but does not know it on account of the static quality of his surroundings and other times when observing witnesses fail to recognize unconsciousness that the patient is aware of because his actions appear to be normal Obviously a definition is essential This has been made available only recently by Cobb He emphasizes that consciousness is a *manifestation of the organism while in action* It is made up of many elements must of necessity have many degrees and must be integrated at many levels Thus one form of consciousness which we commonly recognize includes the integrated functioning of such basic attributes as respiration and the maintenance of circulation with the individual ability to read an absorbing book Such a person will be conscious in one sense but to the man who is being robbed around the corner from him and whose cries for aid do not penetrate the concentrated attention of the reader the latter is to all intents and purposes unconscious At the other extreme is the individual whose only connection with his surroundings as far as the observers know is the maintenance of his circulation and respiration Thus it can be seen that there is neither ever any state which is actually full consciousness nor any condition short of actual death when there is full unconsciousness This concept of consciousness and its loss includes all the stages that have been popularized under such terms as dizziness blackness being dazed being confused response or lack of response to varying degrees of painful stimuli and so forth With this in mind the doctor will never be content to accept the patient s assertion that he was either conscious or unconscious after an accident He will put such a statement to the test from the point of view of the impairment of the patient s contact with his surroundings in all spheres of mental as well as physical activity To do this successfully will require

Direct and Contre coup Damage

Much has been made in the past of the importance of contre coup damage to the surface of the brain Knowledge of its presence is important as a measure of the extent of the surface damage to the cerebrum or as a potential site for the source of a subdural hematoma The importance of the first fades into relative insignificance from a therapeutic point of view when it is considered in relation to the much more widespread and more damaging subcortical changes In the latter case little practical significance can be attached to the knowledge since the final diagnosis of any subdural hematoma must rest on a bilateral exploratory trephination

Academically however it is known that contre coup damage to the surface of the brain of whatever grade only takes place when the injury is caused by the forcible contact of the moving skull against a stationary object The local direct damage occurs on the surface of the cerebrum immediately opposite the point of contact The contre coup damage is located on the surface of the brain at a point corresponding to the opposite extremity of the hypothetical chord which originates at the point of impact of the blow and subtends the longest and flattest arc of the cranial vault

With the skull and its contained brain both in motion in the same direction the brain because of its relatively greater inertia lags slightly behind the bone At the moment of impact the apex of the arc in question either bends outward or breaks This permits its distal extremity to move sharply inward against the surface of the lagging cerebrum The amount of damage done to the latter organ will depend upon the amount of inertia of the brain the weakness of the bony arch and the abruptness with which the motion is arrested

The History and the Examination

There are certain essential historical and physical data that must be obtained in every case of cranio cerebral injury before the ultimate diagnosis can be made There are other data which may be obtained notably in connection with such special examinations as the making of x ray films of the skull the immediate procurance of which popularly is supposed to be essential but which is not only useless but subjects the patient to undue risk An understanding of these points is requisite to the proper management of the condition whether the ultimate therapeusis is operable or non operable

if the therapy has been bad Because it is a subjective rather than an objective symptom it must be inquired about if possible without the putting of leading questions In the later stages of untreated or badly treated cerebral injuries it appears as an afternoon or evening symptom It may be located at any point in the cranium Exertion mental activity emotional stress and liquor all tend to make it worse Its presence reacts unfavorably on the patient s morale and often makes him exaggerate the frequency and severity of this symptom Amnesia or loss of memory also will militate at times against obtaining an adequate and correct history in these older cases The loss of memory in respect to length and relation to the accident varies from nothing up to a period that antedates the accident by some 24 or more hours or weeks afterward If it can be shown unquestionably that the amnesic period started with and followed the accident a period of unconsciousness may be predicated The doctor should be especially careful however to verify adequately all claims of amnesia that might have legal implications in order to avoid being a party to any intentional deceit by the patient

Examination

In all patients with cranio cerebral injuries there are certain essential objective data that must be determined These as with the history are fundamental and apply to any such case The first is the measurement of the patient s blood *pressure* Both diastolic and systolic readings should be taken From these and the calculated pulse pressure it can be *determined* at once whether or not the patient is in surgical shock If it is decided that surgical shock does complicate the picture then all further measures other than those *directed* toward its correction are contra indicated When surgical shock is not present then the examination can be carried further The second procedure should determine the presence or absence of associated major injuries These two when taken together with the history will give the doctor the best information in the least time about the patient s general condition

Next in importance to evaluating the patient s *general* condition comes the settlement of the question as to whether or not the cranial injury is one that will permit the *introduction* of infection into the cranial cavity This in the majority of instances necessitates a scalp wound at least and an open exposure of the brain tissue at most The scalp wound alone providing the periosteum is intact is no more than a scalp wound even though a fracture of the bone lies beneath the intact periosteum If the periosteum is broken however and the fracture exposed through the tear

a considerable degree of lawyer like cross questioning However when doing this the physician should studiously avoid any appearance of attempting to fix the legal responsibility for the damage This does not come properly within his province and attempts to include it as part of his medical data will lead him into difficulties all too frequently It should be obvious in this connection that the actual mechanics of the injury are of no importance in the treatment of the patient The acquirement of these data lead to a wasting of valuable time After all a patient dies as completely from an undiagnosed and untreated cerebral lesion whether it was caused by a fall on a wooden floor or by an automobile accident

Having demonstrated a loss of consciousness it is important to ascertain next whether or not there was a conscious interval If it can be shown that such an interval was present it must be considered as pathognomonic evidence of cerebral extra or sub dural hematoma until proved otherwise During the conscious interval the patient normally is in contact with his surroundings and may be unless cross questioned entirely unaware of the fact that unconsciousness preceded this state An historical sequence of a blow on the head followed by a period of consciousness which in turn is succeeded by a period of advancing coma should be regarded as suspiciously as though a period of unconsciousness immediately following the receipt of the blow had been included in the description

The history will prove a useful means of checking on the possible presence of such extraneous objective factors as may be expected to lead to complications of the cerebral injury Chief among these are toxic dehydration and exhaustion Vomiting and exposure to heat whether from the sun or from injudiciously applied coverings and especially if combined with intended or accidental limitation of the fluid intake lead to the first Exposure to cold long journeys and associated major injuries lead to the latter

When taking the patient s history at any appreciable interval after the injury the facts as given should be scrutinized with more than usual care Intentional and unintentional misstatements abound Financial and legal complications have arisen the attitude has become emotional rather than rational and it may prove impossible to get data in regard to the presence of unconsciousness that is reliable In such circumstances the doctor may find it helpful to determine whether or not the patient had a headache after the accident and if so for how long and to what extent Such a symptom developing shortly after the accident and lasting steadily for a few hours up to a number of days is an almost invariable accompaniment of any cerebral injury greater than concussion It lasts longer

subarachnoid space In deeply comatose patients this can be done without difficulty and the figures obtained with considerable accuracy If the patient is uncooperative and restless however the procedure is much more difficult and the readings much less accurate Under these latter circumstances the lowest reading should be taken as an approximation of the intracranial pressure Although admittedly an approximation this level will serve to indicate the need for and the amount of fluid to be withdrawn as a therapeutic measure and this same puncture thus can be used as an aid in treatment as well as for diagnosis The amount of cerebrospinal fluid to be withdrawn will depend upon the consequent reduction in intracranial pressure but even in those cases in which from dehydration exhaustion or other cause the pressure is below normal originally enough fluid should be collected not more than ½ c c so that a gross estimate of its color and therefore blood content can be made Attempts to estimate the intracranial pressure by counting the rate of drops from the needle or by guessing at the length of the spurt of fluid from the same source are indefensible and should never be made Failure to determine the complicating presence of surgical shock or the possibility of toxic dehydration before measuring intracranial pressure will lead to misinterpretation of the significance of the figures that are obtained Thus a reading of 150 mm of water on the manometer should be interpreted as normal in the absence of these two factors but in their presence may represent not a normal level of pressure but one artificially lowered from its true level of 300 mm of water Such a reading implies not only a different progno is but also different therapy

Thus far the examination has been devoted to the determination of certain data that is essential if the doctor s future therapy is to be properly conceived and carried out None can be omitted and for the purposes of immediate treatment nothing further need be done if the patient s condition contra indicates it However if a more extensive examination is permissible one should recognize its limitations and avoid a cribing too much importance to the individual sign From the remaining procedures one can hope only to determine the approximate location of the greatest amount of brain injury and some idea of the prognosis as far as life expectancy is concerned For these purposes resort must be had to a study of x ray films of the skull and of the abnormal signs that can be elicited by a neurological examination

Roentgenology — To get the full benefit of x ray films it is essential that the physician and the roentgenologist work in cooperation The doctor should not ask the x ray technician to take films when the patient is uncooperative confused or in surgical shock Neither should the roent

the graver diagnosis of compound fracture must be made This latter implies that infectious material has already entered the bone and is in contact with the dura or even the deeper structures This important diagnostic differentiation can be carried out most accurately if the examiner will insert his sterile finger through the scalp wound and palpate the suspected bone directly This method is infinitely more accurate than the use of instruments, retractors or lights and should be used whenever the question of a compounding of a fracture of the skull arises No hesitation should be felt about removing the sutures from a wound already closed nor about enlarging a small scalp wound to a point where it will admit the examiner s finger It is better for the patient to have an unnecessary scar in his scalp than to develop meningitis or a brain abscess because the compounding of a fracture was missed through lack of adequate examination To do this it is not only not necessary but unwise to shave the scalp or attempt to clean the wound at this time (see Compound Fracture) If a compound fracture is present its treatment takes precedence over that for any other associated pathology The remaining modes of entry of infection are found in fractures through the cribriform plate into the nose through the walls of any of the air sinuses but especially the frontal and through the temporal bone into the external ear The first is a serious surgical complication that requires operative relief at the earliest moment that is safe It is diagnosed by the demonstrating of leakage of cerebrospinal fluid from the nose either through the posterior nares into the pharynx or the anterior nares onto the upper lip The other two types of fractures do not require emergency treatment and their detailed diagnosis can be safely postponed in the former case until adequate x ray examination can be made and in the latter until more complete data relative to the intra cranial pressure has been collected

Having made a rough estimate of the patient s general condition and determined whether or not potential sepsis and surgical shock are to be factors in future therapy a decision must be arrived at next in regard to the measurement of the patient s intracranial pressure and the determination of the presence of blood in his cerebrospinal fluid In the absence of surgical shock and a scalp wound this knowledge is indispensable at once In the absence of surgical shock but in the presence of a compound fracture of the skull it is extremely useful but not immediately indispensable In the presence of surgical shock its acquisition should be postponed until after the shock has been corrected The intracranial pressure can be measured in cranio-cerebral injuries only by a manometer attached to a lumbar puncture needle which has been inserted into the patient s lumbar

is of no diagnostic significance in these acute injury cases after the patient is more than two years old

The Localization of the Point of Maximum Brain Injury — This usually is impossible except as an approximation Since any or all signs may be completely misleading at times the best that one can hope to do is to lateralize the injury Its placement in the anteroposterior direction can be little more than a guess To do even this a careful neurological examination is essential Experience has shown that if in the course of this examination certains signs are elicited they can be allowed to carry a little more localizing or prognostic weight than the average Those of localizing significance are (1) A generalized rigidity in extension This means decerebration from extensive mid brain damage The prognosis is inevitably fatal ( ) Aphasia This must be interpreted however in the light of the patient s right or left handedness and especially from the point of view of language difficulty due to lack of education or foreign birth It points to a temporofrontal lesion (3) A facial palsy of the central type This either alone or in combination with aphasia has indicated the side of the subdural hematoma with considerable frequency (4) Dilatation of one pupil This is an unreliable localizing sign It has been shown to occur as frequently opposite to as on the same side as the brain lesion (5) Pathological reflexes These are not reliable indicators even if they are unilateral (6) A hemiplegia This may be present on the same side as an expanding lesion as well as on the opposite side This confusion arises because the brain is moved laterally by the big clots far enough to allow the opposite edge of the tentorial incisura to compress the opposite pyramidal tract before its fibres cross in the pons (7) Complete blindness with a loss of the light reflex in one eye means a division of that optic nerve anterior to the chiasm (8) Papilledema is rare before 10 to 14 days after the injury (9) A stiff neck may be due to blood and not infection in the meningeal spaces

From the prognostic point of view the following may be helpful (1) The depth of coma This is an indication of the severity of the injury but has no further prognostic significance It should be measured by the patient s response to definite purposeful stimuli (2) General muscular flaccidity and (3) relaxation of the anal sphincter both are very bad prognostic signs (4) Retention of urine with an overflow bladder is unfavorable but (5) periodic complete emptying of the bladder usually indicates a lessening of the coma (6) Sudden fixed dilatation of both pupils is a terminal symptom (7) Respiratory irregularity especially if it succeeds stertor and is followed by any type of Cheyne Stokes rhythmicity means an advancing lesion which usually will terminate in

viding no harm is done in order that the patient may not be deprived of objective evidence of having been injured

Any films other than the two special flat views mentioned above that are taken to demonstrate cranial injuries must conform to certain standards If they do not neither the surgeon nor the roentgenologist should attempt to make a diagnosis from them The individual films must be contrasting black and white and not gray films They must show not only the fracture line if any but the grooves for the meningeal arteries and the larger sinuses as well The lateral views must be a true lateral that is the internal acoustic meati must overlap and the anteroposterior ones must be so taken as to be actually in the sagittal plane that is the images of the rami of the lower jaws must be duplicates No less than six films must be taken Stereoscopic views from either side and single A-P and P-A films are the minimum Views of the foramen magnum have not proved helpful in my experience However views taken to show the position of the calcified pineal gland may be very useful

Information other than that relative to the presence or absence of a fracture of the bone and its relation to vascular markings and air sinuses is not ordinarily obtainable from x ray films The exceptions occur in association with the calcification of an intracranial clot usually subdural the comminution of the fracture of no therapeutic significance the coincidence of the fracture with a suture line commonly miscalled diastasic fracture the misinterpretation of the normal forking at the mastoid end of the lamdoidal suture as a fracture line and the attribution of diagnostic significance to scalloping or convolutional markings in the film despite the fact that their etiology is unknown and their presence demonstrably coincidental

X rays taken long after the receipt of the skull injury may be subject to dispute as to their value as evidence of fracture It will be claimed that the predicated fracture line is invisible at a later date because the bone has healed in the interval This is an undoubted possibility It is more likely to happen in children than in adults in linear as opposed to other types of fractures and if the pericranium has been kept intact than if it has not Even depressed fractures have been known rarely to be sure to have healed in such a way as to produce what is to all appearances a normally intact inner table The time necessary to effect complete healing in any cranial fracture varies from months to years and it may never take place at all Fibrous union however always takes place and from the point of view of function is as satisfactory as the bony type Fracture lines in which the dura is incarcerated never heal at that point as far as is known until the dura is removed Separation of the sutures

made by the conversation of anxious relatives and friends. If possible they should be excluded from the patient's room until he is again rational. If this proves to be impossible they should be so placed that he cannot see them and they must be absolutely silent. Bright light has the same stimulating effect that noise has. This applies particularly to sunlight and unshielded electric lights. They and other similar sources of illumination should be excluded insofar as possible. External heat should be applied to the patient only when he is cold. Thus it should not be used in the face of a high temperature even though the clinical diagnosis may be surgical shock. The resultant sweating and other loss of body fluids well may add a complicating toxic dehydration to a situation that is already complex enough. Reduction of abnormally high temperatures such as those seen in association with the hyperthermia of medullary edema may be attempted but usually is of little avail. However attempts should not include cold sponges or cold packs. Such applications contract all surface vessels. The only possible means of reducing these high temperatures inside the body is by the transfer of the heat therein to and its subsequent irradiation from the surface. The transfer is by means of the blood stream and the irradiation is from the surface vessels. Both these processes will be facilitated by procedures which dilate the surface vessels and impeded by those that contract them. The preferred method of dealing with such hyperthermia is to keep the surface of the body moist with fluid at normal body temperature. This will insure the delivery of blood to the surface. This in combination with some method for evaporating this fluid will promote irradiation and thus cooling. Exposure of the wet body to a gentle breeze from an electric fan fulfills these conditions. Temperatures can be reduced in this way 5 or 6° in an hour. It is customary to apply an ice cap to the head of all patients suffering from a cranio-cerebral injury. My experience has been that this procedure is without therapeutic merit. Its only conceivable use is to render the patient willing to keep his head somewhat quieter than he would otherwise because of his subconscious desire to successfully balance the cap and to thus avoid the imagined disorder that might follow its fall.

Position of Patient

A comptetent nurse will never permit her patient to remain in an awkward or uncomfortable position unless forced to do so because of necessary restraints. If there are paralyzed extremities this precaution is doubly necessary. Over flexion of the hands at the wrist, over extension of the feet at the ankles, embarrassment of respiratory movements from

death within a few hours It is due to medullary edema (8) Circulatory failure more particularly in old people usually is evidenced by peripheral cyanosis and at the end by edema and what appears to be a bronchopneumonic process in the lungs There may be no cardiac irregularity except at the end The pathology seems to be primarily that of increasing tissue anoxemia Arteriosclerosis with previous irregular methods of living anemia inhalation anesthetics the administration of large amounts of barbiturates and frequently accidental or therapeutic toxic dehydration all predispose to this condition It is an extremely bad prognostic sign

General Principles of Treatment

There are certain general principles of treatment that apply to all patients with cranio cerebral injuries regardless of the individual pathology They have to do with nursing problems the care of the skin and viscera the necessary use of drugs and the therapy that arises out of those miscellaneous complications produced as the result of various nerve palsies They should not be neglected in favor of the more spectacular procedures that apply more directly to the pathology itself

Nursing

The presence of a competent nurse in attendance on a patient with a cranio cerebral injury may make the difference between a recovery and a fatality This does not imply a knowledge of drugs or medicine or surgery on her part but it does imply the ability to control her patient with a minimum of mechanical aid to eliminate such harmful influences as excessive noise or light to recognize the importance of a wet bed unnatural positions of paralyzed limbs and the early development of contractures and to control family and friends from the point of view of the best interests of the patient All or any of these requirements necessitate an even temperament a sense of the importance of little things and a willingness to subordinate what might be called the profession to the art of nursing

Noise Light Heat and Cold

Patients with cranio cerebral injuries are particularly susceptible to the effect of external stimuli The absence of noise about such an individual makes it much easier to keep him quiet and therefore provides him with a better chance to recover Included among noises must be that

made by the conversation of anxious relatives and friends. If possible they should be excluded from the patient's room until he is again rational. If this proves to be impossible they should be so placed that he cannot see them and they must be absolutely silent. Bright light has the same stimulating effect that noise has. This applies particularly to sunlight and unshielded electric lights. They and other similar sources of illumination should be excluded insofar as possible. External heat should be applied to the patient only when he is cold. Thus it should not be used in the face of a high temperature even though the clinical diagnosis may be surgical shock. The resultant sweating and other loss of body fluid well may add a complicating toxic dehydration to a situation that is already complex enough. Reduction of abnormally high temperatures such as those seen in association with the hyperthermia of medullary edema may be attempted but usually is of little avail. However, attempts should not include cold sponges or cold packs. Such applications contract all surface vessels. The only possible means of reducing these high temperatures inside the body is by the transfer of the heat therein to, and its subsequent irradiation from the surface. The transfer is by means of the blood stream and the irradiation is from the surface vessels. Both these processes will be facilitated by procedures which dilate the surface vessels and impeded by those that contract them. The preferred method of dealing with such hyperthermia is to keep the surface of the body moist with fluid at normal body temperature. This will insure the delivery of blood to the surface. This, in combination with some method for evaporating this fluid, will promote irradiation and thus cooling. Exposure of the wet body to a gentle breeze from an electric fan fulfills these conditions. Temperatures can be reduced in this way 5 or 6 in an hour. It is customary to apply an ice-cap to the head of all patients suffering from a cranio-cerebral injury. My experience has been that this procedure is without therapeutic merit. Its only conceivable use is to render the patient willing to keep his head somewhat quieter than he would otherwise because of his subconscious desire to successfully balance the cap and to thus avoid the imagined disorder that might follow its fall.

Position of Patient

A comptetent nurse will never permit her patient to remain in an awkward or uncomfortable position unless forced to do so because of necessary restraints. If there are paralyzed extremities this precaution is doubly necessary. Over flexion of the hands at the wrist, over-extension of the feet at the ankles, embarrassment of respiratory movements from

the weight of a paralyzed arm which is lying on the chest or abdomen and the imposition of the weight of the body on an arm or leg for even the shortest amount of time all must be constantly watched for and studiously avoided A cradle always should be placed in such a way as to keep the bed clothes off the feet Any signs of contracture should be reported at once in order that appropriate corrective apparatus can be applied early There is disagreement as to whether such a patient s head should be kept above or below the level of his pelvis Those who advocate the head high position claim that it reduces intracranial pressure because of the effect of gravity on the cerebrospinal fluid On the other hand their opponents claim that such a position compresses the jugular bulbs under the weight of the brain and promotes cranial venous congestion and thus increases intracranial pressure These latter believe therefore that the patient s head should be lower than his pelvis My experience leads me to believe that in young conscious cooperative patients that position which is most comfortable is the preferable one This usually means the head low There need be no hesitation however in changing to the head high if the patient wants to In all other cases the position of the head in relation to the pelvis depends upon such factors as the circulation respiration paralysis of deglutition other injuries and so forth It is especially important however to see to it that elderly patients are placed in a sitting position in bed at the earliest possible moment

Restraints

It can be stated as a general rule that in patients with cranio cerebral injuries the fewer restraints the better Their use should be only for the purpose of preventing the patient from doing himself harm This will include preventing him from falling or getting out of bed from removing dressings over wounds splints from his extremities intravenous drip needles from his veins and the stomach tube from his stomach Within these limits he may have and will do better if he has complete freedom of motion When applied the restraints should be efficient and should accomplish only the purpose for which they are put on and nothing more The use of a strait jacket to keep him from taking off a bandage for example cannot be condemned too strongly The production of such artificial immobility in this or any other way defeats the purpose of restraint Immobility is accomplished only after the patient has fought himself into a state of exhaustion in his efforts to escape Thus he has harmed himself much more than he could possibly have done if he had been given complete freedom Whether used with or without mechanical

and the influence of the nurse must not be neglected. If she will exercise a little tact and gentle persuasiveness, if she will be patient and entirely reasonable and unemotional at all times, it will only be necessary to use a minimum of mechanical aid to effect reasonable limitation of activity. In particular it should be emphasized that it is absolutely inexcusable to combat the patient's lack of cooperation by brute force.

There are many types of acceptable restraints. The most useful are bed sides. They may be of metal, wood or canvas. I no longer use anything but canvas. This type comes in two pieces and is made from heavy awning material or sail cloth. Each piece measures 6 feet in length and slopes from a width of 28 inches at the head of the bed to a width of 18 inches at the other end. All edges are perforated by metal lined holes at appropriate intervals. When in use, the outer edge of each piece of canvas is laced to the bed frame and the lower and upper ends to the foot and head pieces respectively. The centre edges are then tied together at their lower ends and thereafter pulled together with lacing as high up toward the head of the bed as is necessary in order to keep the patient beneath them. Rope is the best lacing material. If the patient persists in crawling out from under this and getting out of bed, it will be necessary to restrain his feet. This is done by wrapping the ankles with flannel over which is tied folded sheeting. The free ends of the sheeting are fastened to the foot piece of the bed at its midpoint and with the feet close together. The hands can be restrained in a similar way except that the sheeting should be tied to the bed frame at either side. Extremely obstreperous cases may have to have a folded sheet pulled tightly across their chest, or thighs, or both, and then fastened to the bed frame on either side. This should constitute the maximum, however, and should be needed rarely and then for short periods of time only.

Care of the Skin, Mouth, Lips, Teeth and Hair

The condition of the patient's skin, especially over weight bearing bony points, has long been recognized as the test of successful nursing. This has been particularly true in regard to individuals with spinal injuries and holds no less true in relation to those with severe cranio cerebral damage. The lesions of the skin, when they develop, range all the way from a transitory redness over bony prominences to an actual loss of tissue from ulceration and secondary infection. The skin over the sacrum, the iliac crests, the heels, elbows, the region of the scapulæ, the back of the head and even the upper dorsal spinous processes are the sites that are most commonly involved. Local applications vary with the nurse and nursing

school and all that I have seen in use have proved equally satisfactory None of them however can be or are satisfactory unless certain basic requirements are met These are three The most important is the prevention of maceration of the skin Maceration follows pressure on wet skin It may develop within 30 minutes in favorable cases To avoid it the bed must be kept constantly dry If it gets wet it must be changed at once the wet skin washed dried rubbed with alcohol and well powdered Next in importance is the prevention of excess local pressure over any bony prominences This is most apt to develop in hemiplegic or comatose patients To prevent it the patient must have his position constantly shifted This should be done on schedule and in such a way that all weight bearing points share equally I have found that air rings or homemade doughnuts are not only not satisfactory but are harmful Instead I use a single lambskin tanned with the wool on and with the wool side against the skin This is placed beneath the buttocks and lower back It should be washed sterilized in lysol solution and then dried before use If two or more are available dirty skins can be replaced at once and yet a clean one be always available Smaller pieces may be used also under other points of pressure such as the heels back of the head and so forth Finally skin irritation from friction must be avoided This is prone to develop in restless uncooperative patients and is most apt to affect the shoulder blades elbows and the back of the head The local use of a piece of lambskin as noted above constant nursing attention and such therapy as will take care of the underlying brain pathology are the best methods of care and prevention

Much comfort is derived from adequate care of the mouth lips and teeth They should be cleaned regularly, and the lips in particular should be kept soft and free from sores

The hair especially in women must not be neglected When it is long and tangled matted with blood or vomitus or allowed to remain undisturbed beneath a bandage it is a source of worry and great discomfort to its owner It should be combed and cleaned the worst parts being sacrificed if necessary and bandages if any so applied as not to include long hair if it is at all possible Daily care thereafter should prevent any recurrence of this disorder

Food and Fluids

There is no limit to the type or quantity of food that these patients may be given other than its caloric chemical or vitamin content and their capacity and willingness to eat it.

It is essential in the care of these cranio cerebral injury cases to have some knowledge of their fluid intake and output In the case of the out put this can only be an approximation but even so the figures are signifi cant and helpful The measurements should be for 24 hour periods in either c c or ounces They should then be plotted on the temperature or other chart in the form of a graph Much of their significance is lacking otherwise *The amount of fluid intake per 24 hour period should be speci fied by the physician* The nurse however carries the responsibility of seeing that the patient takes that amount and also of collecting measuring and recording the fluid he puts out Fluid is best administered by mouth and need not necessarily be limited to varieties that have no caloric or vitamin content Oral administration can be supplemented by intrave nous drip subpectoral infusions in small children by intraperitoneal in fusions or clysis and finally with the aid of a Rehfuss or similar tube inserted through the nose

Care of the Urinary Bladder

Although anatomical abnormalities of the urinary bladder are not associated with cranio cerebral injuries except possibly in the ante mortem state micturition does not necessarily take place in a normal manner when there is any significant loss of consciousness This probably is due to a psychological inhibition of the emptying contractions and results in the production of an over flow bladder with retention This must be un comfortable and does actually produce a high degree of restlessness which is promptly relieved by catheterization If the unconsciousness continues for a long time and repeated catheterizations are necessary it is better to make use of a tidal drainage apparatus Although this requires an indwelling urethral catheter it prevents the accumulation of residual urine and the atony that is associated with overstretching of the bladder wall The cystitis that necessarily accompanies an indwelling catheter after 72 hours is of no moment as long as no residual urine collects It will clear up in a few days after the catheter has been removed

When loss of consciousness is so profound however as to exclude any action on the spinal reflexes by the higher centres the bladder becomes a pure reflex type Under such circumstances it will empty completely in response to a given amount of fill This will occur inevitably and regard less of the time element Repeated catheterization therefore is notori ously unsuccessful as a means of keeping such cases dry They can only be handled by being put on tidal drainage and the sooner that is done the less likely they are to have bed sores

In moribund patients the bladder reverts to the atonic form, the external sphincter is flaccid and an overflow retention is present

Care of the Large Bowel

The care of the large bowel presents no extraordinary problem The proper use of enemata and cathartics will assure normal functioning Care should be exercised to make sure that an impaction does not occur in the rectum Incontinence is an ante mortem symptom associated with a flaccid anal sphincter

Care of the Eyes

The final responsibility for the care of injuries to the orbit or its contents in patients with cranio cerebral injuries should be placed on the shoulders of a consulting ophthalmologist Orbital periorbital and subconjunctival hematomas are frequent and if carelessly or improperly treated may lead to permanent impairment of the patient s sight from corneal scars If in addition there is protrusion of the eye ball severe conjunctival edema or chemosis this danger is materially increased Temporary therapy should include the instillation of sterile oil into the conjunctival sac the assurance of an abundant supply of moisture to the conjunctiva if it is dry by the application of an air tight goggle the use of cold compresses locally to reduce the swelling and especially the avoidance of direct contact between the cornea and compresses or bandages An associated facial or trigeminal palsy renders such measures and the care used in applying them until the arrival of the ophthalmologist doubly important

Care of the Ears

If as a complication of a cranio cerebral injury there is blood or cerebrospinal fluid draining either alone or as a mixture from the patient s ear or ears great care must be taken to prevent the entrance of infection into the meningeal spaces through any fracture that may be present To accomplish this it is of utmost importance that the ear canal be neither irrigated nor packed If the former is done infection may be washed in and if the latter infection that is already present in the inner or middle ear and that would otherwise cause no trouble may be dammed up sufficiently to cause it to spread inward rather than drain outward Blood clots in the canal should not be disturbed until all drainage has been ab

sent for 10 days and then only with the greatest of care and preferably by an aural consultant Cerebrospinal fluid drainage is best controlled by measures such as repeated lumbar drainage that reduce the intracranial pressure to normal and keep it there While it is theoretically possible for a permanent aural cerebrospinal fistula to form and require closure by operation I have never seen it It is important to remember that with rare exceptions persistent leakage of cerebrospinal fluid from the ear does not decompress the brain but instead is evidence of persistent high intra cranial pressure

There is no treatment for the deafness that may follow these injuries

Traumatic or hemorrhagic labyrinthitis may be associated with cranio cerebral injuries It tends to get well of itself and is due to a fracture and hemorrhage into the internal ear Vertigo especially on turning the head is the usual evidence of its presence If it persists and provided the disability is extreme a section of the vestibular nerve in the posterior fossa of the skull may be expected to give some measure of relief This should not be undertaken until at least 8 to 12 months after the injury

A loss of the sense of taste frequently is associated with cranial fractures that involve the ear and tends to be permanent There is no treatment

Care of the Nose

Either bleeding or leakage of cerebrospinal fluid from the nose in as sociation with cranio cerebral injuries is an extremely important sign The latter inevitably points to a fracture so placed that the cavity of the nose is in direct communication with the meninges and brain As long as such a fistula remains open meningitis at some time is a certainty It can only be closed by a major operative procedure which nevertheless must be carried out at the earliest moment that the patient s condition permits This fracture usually is in part at least through the cribriform plate and the fistula exists because an open funnel of dura and arachnoid has been caught and incarcerated in the fracture line Lumbar punctures will neither close this fistula nor stop the rhinorrhœa Unlike the ear fistulæ enough cerebrospinal fluid may be lost through leakage to reduce the in tracranial pressure to very low levels even in the total absence of lumbar drainage Until operative closure can be carried out all plugging and irrigation of the nose blowing of the nose sneezing coughing and deep breathing must be prohibited If the patient is kept flat in bed constantly and whenever there is bleeding from the nose the diagnosis may be missed In the former instance the cerebrospinal fluid may leak directly into the posterior pharynx and be swallowed and its presence thus be

In moribund patients the bladder reverts to the atonic form the external sphincter is flaccid and an overflow retention is present

Care of the Large Bowel

The care of the large bowel presents no extraordinary problem The proper use of enemata and cathartics will assure normal functioning Care should be exercised to make sure that an impaction does not occur in the rectum Incontinence is an ante mortem symptom associated with a flaccid anal sphincter

Care of the Eyes

The final responsibility for the care of injuries to the orbit or its contents in patients with cranio cerebral injuries should be placed on the shoulders of a consulting ophthalmologist Orbital periorbital and subconjunctival hematomas are frequent and if carelessly or improperly treated may lead to permanent impairment of the patient s sight from corneal scars If in addition there is protrusion of the eye ball severe conjunctival edema or chemosis this danger is materially increased Temporary therapy should include the instillation of sterile oil into the conjunctival sac the assurance of an abundant supply of moisture to the conjunctiva if it is dry by the application of an air tight goggle the use of cold compresses locally to reduce the swelling and especially the avoidance of direct contact between the cornea and compresses or bandages An associated facial or trigeminal palsy renders such measures and the care used in applying them until the arrival of the ophthalmologist doubly important

Care of the Ears

If as a complication of a cranio cerebral injury there is blood or cerebrospinal fluid draining either alone or as a mixture from the patient s ear or ears great care must be taken to prevent the entrance of infection into the meningeal spaces through any fracture that may be present To accomplish this it is of utmost importance that the ear canal be neither irrigated nor packed If the former is done infection may be washed in and if the latter infection that is already present in the inner or middle ear and that would otherwise cause no trouble may be dammed up sufficiently to cause it to spread inward rather than drain outward Blood clots in the canal should not be disturbed until all drainage has been ab

therapy as is possible is carried out when the causative cerebral lesion is diagnosed properly and therefore treated properly Prognosis in regard to the recovery in any individual instance is unpredictable but hope for resumption of function should not be abandoned for at least a year after the receipt of the injury Treatment after it has been demonstrated that the paralysis is permanent should be left in the hands of a competent ophthalmologist

Division of the optic nerve between the chiasm and the back of the globe occurs fairly frequently It is accompanied by immediate blindness as well as a loss of the light reflex Treatment obviously is of no avail It is important however to recognize the presence of this complication and to notify the patient or his legal representative of it at the earliest possible moment Only in this way can false claims for damages based upon alleged improper treatment by the physician or allegations of fraud and malingering on the part of the patient be combated successfully Above all the physician should not expect the patient to be the one to first recognize his loss of sight

Doubtless any other cranial nerve can be damaged to any degree in association with cranio-cerebral injuries The occurrence rate however is so low except as noted above that detailed discussion of the resulting symptomatology and consequent treatment has no practical value

Drug Treatment

The most important single fact about the use of drugs in the treatment of cranio-cerebral injuries may be epitomized in the following sentence *Never give morphine in the presence of an actual or a suspected increase in intracranial pressure* A usual cause of death in cranio cerebral injuries is a respiratory paralysis which is due to medullary edema and depression of the respiratory centre A usual action of morphine is the depression of the respiratory centre When a patient already is in danger of dying because of a depression of his respiratory centre it is worse than foolish to insure death from respiratory failure even if it is dignified by the name of treatment by administering a drug that acts by depressing the respiratory centre

The over-expenditure of energy by restless patients is however harmful Drugs in addition to treatment directed specifically against the cerebral injury the use of restraints judicious nursing and so forth may be essential to prevent such activity The barbiturate preparations usually prove to be the most useful drugs under such circumstances The ones that are most efficacious are phenobarbital (luminal) by mouth pheno

unnoticed until the patient s head is raised In the latter case the presence of the blood may mask the presence of the fluid The precautions noted above must be observed strictly in the presence of nasal hemorrhage or suspected fractures of the frontal fossa until the absence of this cerebro spinal rhinorrhea can be definitely proven Once the fistula is proven absent or closed by operative procedure ordinary measures to cleanse the nose may be adopted but not before Sulphanilamide in appropriate dosage should be started whenever the presence of rhinorrhea is suspected

The Complications Arising Out of Various Cranial Nerve Palsies

Facial paralysis is a common complication of cranio cerebral injuries It may be either central or peripheral in type usually the latter Its presence calls for particular care of the eye This has been discussed above In addition massage of the facial muscles by stroking upwards from the corner of the mouth toward the outer canthus of the eye, electrical stimulation and if necessary various types of plastic supportive operations on the facial tissues will prove useful If it can be determined that the nerve has been injured in the Fallopian canal it may be decompressed or repaired locally and if this is not feasible or the location of the break not known the distal end may be anastomosed with the proximal end of either the spinal accessory or the glossopharyngeal nerve Neither of these anastomoses is entirely satisfactory, however because when successful the voluntary contraction of the facial muscles is accompanied always by a varying number of associated movements of the shoulder, side of the neck or tongue The more radical operative therapy should never be undertaken unless and until all other procedures have failed completely and only when the surgeon is convinced that the interruption is anatomical and regeneration impossible otherwise

Loss of hearing either with or without loss of sense of taste and dizziness may be associated with *injury to the eighth nerve* These and other points connected with damage to the facial nerve have been discussed sufficiently already under the heading *Care of the Ears*

Oculomotor palsies of all degrees are a common accompaniment of cranio cerebral injuries The most usual is a paralysis of lateral gaze due to injury to one sixth nerve Third nerve palsy may occur also and be manifested at first by a dilatation of the pupil only Ptosis of the upper lid either may appear later or may not develop at all Complete ophthalmoplegia is observed rarely These is no particular treatment of the eyes themselves other than symptomatic that is of any value As much

muscular twitching Both these drugs and especially caffeine are useful in the treatment of a failing circulation or to stimulate respiration Strychnine is useful in case of barbiturate poisoning and will prove useful in bringing the deeply comatose patient closer to the conscious level *Coramine* is a drug for strictly emergency use It is given intravenously and the dose is 1 ampoule The ampoule contains 5 c c of a 25 per cent aqueous solution It is a strong respiratory excitant and is helpful in tiding over a sudden respiratory emergency which will be ended by a decompression a ventricular puncture or some similar procedure I have never used more than one ampoule

METHODS OF TREATMENT

In addition to the general methods of treatment necessary for the care of any major or minor surgical condition there are certain special procedures that are peculiar to the care of patients suffering from cranio cerebral injuries For convenience of reference all of these are grouped in this one section No attempt will be made to relate any special procedure to any given type of injury That will be covered in succeeding sections which deal with the individual injuries under appropriate diagnostic headings In general methods of treatment of cranio cerebral injuries are either operative or non-operative The non-operative procedure will be dealt with first and in some detail Operative methods will not be described since the more detailed technical minutiae are peculiar to the needs of the surgeon in contradistinction to those of the physician

Non operative Methods of Treatment

Lumbar Puncture — The most universally applicable therapeutic and an indispensable diagnostic procedure for handling any and all types of cranio cerebral injuries is the lumbar puncture In acute injuries of the skull and its contents its use is entirely without danger regardless of the degree of intracranial pressure Many thousands of lumbar punctures have now been done in such cases and no verified case has come to light in which it has been shown by post mortem or equally accurate study that the lumbar puncture did in fact cause death From the point of view of therapy it has been shown by a study of two parallel series of cases treated by all members of the surgical staff of a large municipal hospital that an increase in the therapeutic use of lumbar puncture of only 4 per cent was associated with a decrease in mortality of about 13 per cent The total number of cases studied was 983 and the period covered 4 years

barbital sodium (luminal sodium) intravenously and pentobarbital sodium (nembutal intravenous) intravenously All of these when given by mouth will act more slowly but over a longer period of time than when given by vein The usual dosage follows — Phenobarbital gr 1½ (0 1 gm) by mouth 2 or 3 times a day Phenobarbital sodium enough intra venously to produce immediate sleep as much as gr 10 (0 6 gm) has been given in this way in an adult but this is unquestionably a high maximal dose Pentobarbital sodium enough intravenously to produce immediate sleep less than gr 7 (0 5 gm) for an adult usually is required Strychnine is to be given in case of an overdose of barbiturates It should be given in doses of gr 1/30 (2 mgm) intravenously and repeated as indicated There is at present some evidence to show that excessive use of the bar biturates can produce a toxic anoxemia which in certain cases will prove fatal

Paraldehyde by rectum or in extreme cases intravenously is a useful soporific Dr 6 to 8 (24 to 32 c c) in 4 ounces (120 c c) of starch solu tion is the adult dose when given by rectum and an average of 1 dr (4 c c) but not more than 2 dr (8 c c) in a single dose when given intra venously

For headache a combination of codein gr ½ (30 mgm) aspirin gr 10 (0 6 gm) frequently will be effective after all other and more complicated remedies have failed This dose can be repeated every 4 hours until relief is obtained Tribromethanol (avertin) is contra indicated in these cases except when used as a basal anesthetic Sulphanilamide (prontolin) should be given whenever an infection with a *streptococcus hemolyticus* or a *meningococcus* is either suspected or proved The dosage must be suffi ciently large at first and then so graded as to produce and maintain a concentration in the blood at 10 mgm per cent or higher In men ingococcus meningitis it is well to use antimeningococcus serum beside sulphanilamide It may prove useful too when treating *pneumococcus men ingitis* especially if proper type specific serum also is available and used With all of these infections the blood concentration of the sulphanilamide must be kept at the higher levels so long as severe symptoms of toxicity of the drug do not develop

The most dependable stimulants are caffeine strychnine and coramine *Caffeine* should be given intravenously in 7½ grain (0 5 gm) doses This may be repeated every 2 hours or oftener It is of absolutely no use when given in any other way *Strychnine* also should be given intrave nously The dose should be gr 1/30 (2 mgm) which may be repeated every 2 hours for 4 to 6 doses The amount should be reduced thereafter and care should be taken not to prolong its use to the point of producing

muscular twitching Both these drugs and especially caffeine are useful in the treatment of a failing circulation or to stimulate respiration Strychnine is useful in case of barbiturate poisoning and will prove useful in bringing the deeply comatose patient closer to the conscious level *Coramine* is a drug for strictly emergency use It is given intravenously and the dose is 1 ampoule The ampoule contains 5 c c of a 25 per cent aqueous solution It is a strong respiratory excitant and is helpful in tiding over a sudden respiratory emergency which will be ended by a decompression a ventricular puncture or some similar procedure I have never used more than one ampoule

METHODS OF TREATMENT

In addition to the general methods of treatment necessary for the care of any major or minor surgical condition there are certain special procedures that are peculiar to the care of patients suffering from cranio cerebral injuries For convenience of reference all of these are grouped in this one section No attempt will be made to relate any special procedure to any given type of injury That will be covered in succeeding sections which deal with the individual injuries under appropriate diagnostic headings In general methods of treatment of cranio cerebral injuries are either operative or non-operative The non-operative procedure will be dealt with first and in some detail Operative methods will not be described since the more detailed technical minutiæ are peculiar to the needs of the surgeon in contradistinction to those of the physician

Non operative Methods of Treatment

Lumbar Puncture —The most universally applicable therapeutic and an indispensable diagnostic procedure for handling any and all types of cranio cerebral injuries is the lumbar puncture In acute injuries of the skull and its contents its use is entirely without danger regardless of the degree of intracranial pressure Many thousands of lumbar punctures have now been done in such cases and no verified case has come to light in which it has been shown by post mortem or equally accurate study that the lumbar puncture did in fact cause death From the point of view of therapy *it has been shown by a study of two parallel series of cases treated* by all members of the surgical staff of a large municipal hospital that an increase in the therapeutic use of lumbar puncture of only 4 per cent was associated with a decrease in mortality of about 13 per cent The total number of cases studied was 983 and the period covered 4 years

To be safe and particularly to be either therapeutically or diagnostically significant a lumbar puncture must be done properly proper equipment must be used and the operator must have some idea of what information is obtainable If these criteria are not followed the data will be incomplete inaccurate unreliable and may lead to diagnostic errors that will seriously jeopardize the patient s chances

The Interpretation of Lumbar Puncture Findings — Of all the data made available by a lumbar puncture in a case of cranio cerebral injury that relative to the intracranial pressure is most liable to misinterpretation Since it is known that either surgical shock or toxic dehydration will reduce intracranial pressure to artificially low levels the pressure measurements obtained by lumbar puncture must be considered in the light of these facts Thus, it is essential to have blood pressure readings and an adequate history of the fluid intake This latter must include statements relative to exposure to heat fever vomiting consciousness and if at all possible some estimate of the amount of fluid intake and urinary output for at least one and better more than one 24 hour period If it can be shown that toxic dehydration is a possibility or that surgical shock is present the finding of a subnormal intracranial pressure will confirm that finding a normal reading will point to an actual increase and a high reading to even higher levels of pressure Both prognosis and treatment must be modified accordingly

The finding of white blood cells in the removed specimen of cerebro spinal fluid does not necessarily indicate a meningeal infection The presence of blood in the cerebrospinal fluid may set up a pleocytosis which will clear up after the red corpuscles have been destroyed or removed A better indication for the presence of a meningeal infection is found in a study of the sugar and chloride content of the fluid

If the first lumbar puncture is done some days after the receipt of the injury or after enough time has elapsed to permit the destruction of the red blood cells in the fluid a measurement of the total protein content may serve as an indicator of a previous admixture of blood In the cases with large amounts of added blood the fluid will be yellow but even in those cases in which the added blood has been too small in amount to be grossly visible later as a yellow discoloration its presence may be detected and deduced by and after a measurement of the total protein content

Therapeutic Dehydration

Therapeutic dehydration may be accomplished by the administration of appropriate solutions either by mouth by rectum, by vein and in the

new born intramuscularly Regardless of the method used however the effect on the brain will be limited to a reduction of its volume It is apparent therefore that the intracranial pressure will be reduced only in so far as the brain shrinks and that that modicum of pressure that is due to mechanical blockade of the arachnoidal villi by free blood cells in the subarachnoid fluid cannot and will not be altered

Dehydration by Mouth — This method is of interest only for purposes of record A sufficient number of appropriately sized doses of a saturated solution of magnesium sulphate is given to produce several watery bowel movements in each 24 hour period It is useful for its psychological effect only

Dehydration by Rectum — This method has a distinct place in the therapy of cranio cerebral injuries If a proper technique is used a rather slow and prolonged dehydration can be produced A saturated solution of magnesium sulphate is used the solution being given into the patient s rectum by gravity only Two ounces (60 c c) is the average dose for an adult but this may be varied in either direction The maximum should not exceed 4 ounces however After the solution has been introduced the catheter should be clamped off and left in place The solution need not be warmed before use and there is no necessity for the use of any opium derivative locally On no account should its instillation be preceded by a cleansing enema This procedure may be repeated once every 3 hours for 4 doses or once every 4 hours for 3 doses Twelve hours should intervene between each series regardless of the amount used In the new born no more than 1 drachm of the solution should be given at any one time The drug is not given as an enema The patient should be informed of this and urged to retain his rectal contents as long as possible A note should be made of the length of time the solution is retained Toxic dehydration can be produced by prolonged or injudicious use of this therapy Associated limitation of fluid intake is of no therapeutic value

Dehydration by Vein — This is the most useful and the most rapid method of producing dehydration Ordinarily a 50 per cent solution of glucose is used Because such a solution acts by increasing the tonicity of the blood stream and thus withdrawing by osmosis fluid from the tissue spaces into the vascular tree it is also useful as a means of treating surgical shock Indeed this therapy has proven second only in efficiency to the transfusion of properly matched blood since it raises systolic blood and pulse pressures and prevents further escape of serum through leaking capillaries Hypertonic salt solution originally was recommended as the preferred intravenous dehydrator but experience soon showed that because it was a solution of electrolytes it became isotonic and left the

vascular tree very quickly This served only to increase the tissue edema and to make already bad matters worse More recently certain writers have advocated the use of a solution of sucrose as the preferred intravenous dehydrator The only objection to this is the fact that it is more difficult to obtain when the physician needs it in an emergency in an out of the way place Glucose solution despite reports of animal experimentation to the contrary does not produce a secondary edema like salt solution and unlike sucrose it is obtainable now in an immediately usable form at practically any drug store no matter where located

When glucose is given therapeutically into a vein certain precautions must be observed especially in regard to the commercial solutions The injection must be made slowly and great care should be taken to see that none of the hypertonic solutions get into the perivenous tissues If this happens a considerable degree of sloughing with scars that are disfiguring and slow to heal is liable to follow The syringe should be as nearly as possible chemically as well as surgically clean In particular Ringer s solution should not have been used recently in the syringe nor the syringe wiped with sized cotton cloth or gauze before putting the glucose in it The buffer in the commercial sterile solutions will precipitate if brought into contact with the calcium that is easily mobilized from both Ringer s solution and sizing Such a precipitate may cause severe reactions if introduced into the blood stream of a patient For the same reason if distilled water is used to make solutions of higher dilution it must be free from room dust and have been collected from a dust proof recently emptied still The very hypertonic solutions usually cause thrombosis of the vein at the point of administration Ignorance of this possibility may lead to unnecessary delay in giving subsequent infusions This can often be prevented however by irrigation with salt solution immediately after the injection

As a dehydrating agent in adults hypertonic glucose solution is used in a strength of 50 per cent and in units of 50 or 100 c c In this amount and strength it may be given intravenously every 2 hours for 3 or 4 doses It will have its maximum effect in from 15 to 30 minutes and will gradually cease to act during the next 2 hours Its ill judged or prolonged use will produce toxic dehydration The addition of insulin to this therapy serves no useful purpose

Sterile magnesium sulphate solution may also be used intravenously as a dehydrating agent Its use in this way however should be strictly reserved for those cases that have developed a rapidly advancing malignant edema of the brain This is almost exclusively post operative This therapy puts an enormous extra load on the patient s circulation and if

effective produces a marked toxic dehydration which in its turn must be treated appropriately Furthermore any patient is liable to develop magnesium shock during the administration and preparations must be made in advance to combat this emergency if and when it arises A 2 per cent solution is used It is made by dissolving the crystals in sterile distilled water The dose for an adult is 100 c c of this solution given into any convenient vein by the drop method A skilled nurse or a physician should be constantly in attendance At least 1 hour should be used to give the single dose of 100 c c Before starting a 10 c c ampoule of calcium chloride solution containing 1 gram of the salt (made by Lilly) and an appropriate syringe and needle must be at hand and prepared for immediate emergency use If used this calcium solution must be given slowly also Both solutions must be kept entirely within the vein as any leakage into the surrounding tissues will produce a slough Surgical shock old age or a major circulatory disease are contra indications to its use

Intramuscular Dehydration — Dehydration may be produced in the new born by the intramuscular injection of a sterile magnesium sulphate solution This method is not ordinarily used in children or adults A ½ c c of a sterile 50 per cent solution may be given deeply into the muscles of the buttocks every 3 or 4 hours for no more than 4 doses If the injection is made deeply enough there is little danger of causing a slough

Blood Transfusion

This is a much neglected and very useful procedure in the treatment of many varieties of cranio-cerebral injuries In particular such patients as have associated surgical shock pre and post-operative hemorrhage in addition to extradural bleeding and compound fractures and a late secondary anemia all benefit by this therapy

Surgical shock responds best to small transfusions of 100 to 250 c c each repeated whenever the pulse pressure falls steadily or drops suddenly below 20 mm of mercury To replace lost blood however the amount transfused should be increased to from 250 to 500 c c at any one time

In the new born transfusions are useful in the treatment of so called or suspected hemorrhagic disease as well as for surgical shock Here whole non citrated blood is preferable No typing or grouping of the blood is necessary during the first 10 days of life The donor usually is either parent Thirty to 60 c c commonly is given at each transfusion Any vein other than the superior sagittal sinus may be used The variable position of the latter makes the liability of perforation and the formation of an artificial subdural hematoma too likely for it to be safe Pro-

phylactic transfusions as described are a recognized adjuvant to the treatment of all types of cranio cerebral injuries in the new born

Operative Methods of Treatment

No cranial surgery should ever be done outside of a hospital No cranial surgery should ever be done in any hospital that is not properly equipped for this type of work Obviously such surgery should be done only by one experienced in this form of surgical practice A book intended for physicians not surgeons is not the place for descriptions of technique and procedures of operative surgical treatment

NON OPERABLE GROUP OF CRANIO CEREBRAL INJURIES

Cranio cerebral injuries can be divided into three groups The first two are made up of the non operable and operable cases respectively The third group includes those cases in which the predominant symptomatology is due to important complications of the local injury The pathology of the first group is such that treatment is non operable of the second such that treatment is operable and of the third group is such that before instituting either operable or non operable therapy the associated complications must be corrected or else that as the result of the treatment usually operative further necessary abnormal situations have been produced that in their turn must be treated This is a particularly useful method of classifying cranio cerebral injuries because it depends ultimately for its success on an understanding of the pathology present in any individual case It is inevitable therefore that the treatment and consequently the mortality and morbidity will be improved

The non operable group of cranio cerebral injuries is made up of about 63 per cent of all such hospitalized patients This 63 per cent includes cases of *concussion* (1 per cent) *edema and congestion* (18 per cent) and *contusion* (26 per cent) and *laceration* (17 per cent) These ratios probably are low for the first two and high for the last two because the drift of the severely injured patients is toward and of the less severely injured ones away from hospitals It should be understood clearly that each succeeding diagnosis includes by implication the pathology that has been described under all preceding classifications For example although concussion completely describes the lesion that the patient is suffering from laceration not only describes the predominant tearing of the surface of the brain but implies as well that contusion edema and concussion are present also This concept of the brain

pathology is fundamental The changes occur not only alone but also in some form as an accompaniment of the operable cases and of those classed under complications Indeed if this non operable group is combined with the two commonest forms of operable cases compound fractures and subdural hematoma the combination will be found to include 92 per cent of all cranio-cerebral injuries

Concussion

Pathology — The pathology of concussion is unknown The best acceptable explanation to date is based upon the predication that it is an example of an abnormal response to a vaso vagal reflex This dilates the arterioles of the brain raises intracapillary pressure lowers the general blood pressure and is associated with loss of consciousness If consciousness returns before the chain of events has proceeded further or if the patient s circulation is so efficient that further abnormal progress is prevented he can properly be said to have suffered from concussion In that case such a patient on return to consciousness will present absolutely no subjective or objective symptoms or signs of disease or injury to his brain There may be a fracture of the bones of the skull or any other associated injury but as far as the brain is concerned neurological and mental examinations lumbar puncture and the like will be completely normal and remain so

Symptoms — The symptom of concussion is loss of consciousness immediately following a blow on the head and followed by complete and permanent normality on recovery of consciousness again Any variation from this sequence of events implies a more severe injury and a different diagnosis

Diagnosis — The diagnosis is made on the history together with the total absence of any subjective symptoms or objective signs of injury to the brain other than unconsciousness

Treatment — The disease being self limited by pathology and definition and with complete normality synchronous with recovery of consciousness requires no treatment

Mortality — There is no mortality

Edema and Congestion

These cases have as part of their pathology that described under concussion and the diagnosis to be complete and descriptive, should include this latter term

Pathology — Once the cerebral arterioles and capillaries have been dilated as the result of the vaso vagal reflex which has been predicated as the basic cause of concussion a greater degree of injury or a less efficient circulation will either cause this process to advance or else fail to stop its further development As a result the capillaries leak there is anoxia an overdistention of the perivascular and perineuronals paces and a backing up and congestion of the venous circulation with decreased absorption of the cerebrospinal fluid and an overdistention of the ventricles This is accompanied by a diminution of the size of the subarachnoid spaces There is thus produced an increase in brain volume intra cortical congestion petechial hemorrhages and radial thromboses and an increase in intracranial pressure due to a diminution of the water bed but with normal cerebrospinal fluid

Symptoms and Signs — There is a history of a blow on the head sufficiently severe to produce unconsciousness Following return to consciousness such subjective symptoms as headache dizziness, nausea loss of memory and initiative and inability to concentrate appear The intra cranial pressure frequently will be elevated but the cerebrospinal fluid always will be normal Other objective signs may vary from a single cranial nerve palsy to hemiplegia with convulsions

Diagnosis — The diagnosis is made from the history together with the cerebrospinal fluid findings as outlined above

Treatment — Treatment directed either toward shrinking the brain by dehydration or looking to removal by lumbar drainage of the excess backed up cerebrospinal fluid will be successful Dehydration may be carried out by injecting hypertonic glucose solution intravenously or by the administration of magnesium sulphate by rectum Their efficacy should be checked by the measurement of the intracranial pressure With lumbar drainage enough cerebrospinal fluid should be removed at lumbar puncture to reduce an abnormally high pressure to normal levels This procedure should be repeated every 24 hours until two successive normal pressure measurements have been obtained previous to the withdrawal of any cerebrospinal fluid

The amount of late disability that is caused primarily by earlier edema and congestion of the brain or to any similar pathological state that is initiated by cerebral trauma is not known It is influenced by the treatment that the patient received during both his acute illness and his convalescence Other factors are his economic social and intellectual backgrounds his age and the state of his circulatory system Any one or all of these may influence profoundly the occurrence of late symptoms and mental deterioration and convulsive seizures are among the possible

permanent after-effects The patient s individual liability to any or all of these end results cannot be expressed in figures

Mortality —The mortality should never exceed 1 per cent The associated presence of a non operable injury to the bones of the skull alters neither the diagnosis nor the prognosis

Contusion and Laceration

Cases of contusion and laceration either separately or together include as part of their pathology that described under edema and congestion as well as that under concussion The diagnosis should be modified to suit and it should become customary to include at least in it the words edema and congestion

Pathology — If the cerebral pathology as described above under both concussion and edema is complicated by a bruise of the surface of the brain with a rupture of one or more cortical vessels there is a *contusion* of the brain If the injury has been severe enough actually to tear or lacerate the surface of the brain in addition there is a *laceration* of the brain also Contusions and lacerations of the brain merge into and overlap one another without any sharp distinction except in the extreme cases Ordinarily any differentiation is a purely arbitrary personal one Both are associated with concussion edema and congestion and usually with subcortical hemorrhages as well Both have free blood in the cerebrospinal fluid varying in amount from a few hundred cells in the mildest contusion to practically pure blood in the most severe laceration Intracranial pressure is increased first because of the edema and congestion and secondarily because of the mechanical blockade of the avenues of absorption of cerebrospinal fluid through the arachnoidal villi because of the free red blood cells therein If this increase is marked anemia and then edema of the medulla follow Respiratory failure is associated with the latter and when once present usually proves to be inevitably fatal

Symptoms and Signs — There is a history of a severe blow on the head followed by an unquestionable period of unconsciousness This unconscious period may last for days and can be made to serve as a rough estimate of the severity of the brain injury Loss of sphincter control may be associated with this coma and especially in the moribund cases it is a common experience to find a generalized flaccidity with absent tendon reflexes Respiratory irregularity sudden fixed dilation of the pupils and a sudden increase in pulse rate and temperature occur just prior to death If the injury has been less severe the unconscious period will be followed by a varying degree of disorientation which is accom

panied often by active delirium Nausea and vomiting are common Headache and retrograde amnesia are almost invariable and convulsions and any degree or kind of somatic or cranial nerve palsy can occur Surgical shock invariably accompanies the more severely injured The intracranial pressure is high provided the patient is neither dehydrated nor in surgical shock The cerebrospinal fluid contains free blood in accordance with the amount of damage to the surface of the brain

Diagnosis — The diagnosis is made on the history together with the cerebrospinal fluid findings as outlined above

Treatment — Treatment is most efficient when it consists of a judicious combination of dehydration and lumbar drainage The dehydration will affect only the edema of the brain however and so must be supplemented by a mechanical method such as lumbar drainage to counteract the effects of the mechanical plugging of the openings in the arachnoidal villi The technique is as described under ' Edema and Congestion Operative decompression as a therapeutic measure is contra indicated Exploratory trephination, however is indicated and should be used as a diagnostic procedure whenever the patient fails to improve or gets worse after a suitable amount of non operative treatment such as outlined above (See also under *Treatment* of *Edema and Congestion*)

Mortality — With proper diagnosis and under properly conceived and executed treatment the mortality for this group should never exceed 18 per cent and probably can be kept even lower The presence of an associated bone injury tends to decrease the patient s chances of survival not because the break in the bone is of itself lethal but because the blow that produced it must have been applied with greater force

Concussion edema and contusion or laceration or any combination of them may or may not be associated with any of the specialized forms of cranial bone injury with any type of meningeal hemorrhage and hence with any of the operable group of cases or those whose presenting symptoms place them among the complications All of these latter conditions however will be characterized by their own additional pathological peculiarities and therefore must be considered as separate diagnostic and therefore therapeutic entities

The Operable Group of Cranio cerebral Injuries

The second great group of cranio cerebral injuries is that whose predominant pathology is such that therapy must include operative measures on the cranium It must be understood clearly however that although the predominant pathology is of this particular type it nevertheless over

lies and is present in addition to the fundamental cerebral pathology that has been described in the previous section It is also subject to the complications that are enumerated in the succeeding section

This operable group of cases includes about 37 per cent of all hospitalized cranio cerebral injuries It is made up of sub and extra dural hemorrhages and compound and depressed fractures of the skull The lesions themselves may be expanding non expanding or a combination of both in that order Consequently the intracranial pressures may range from high levels to normal figures Both levels may be present in any one case and yet the lesion be treatable only by operative interference The group mortality is at present about 32 per cent As we become more willing to operate earlier and as our operative technique improves however this figure should be lowered In general treatment must be such as will care properly for the underlying cerebral pathology and in addition avert sepsis control otherwise fatal hemorrhage and obviate later complications without undue risk to the patient Ordinary diagnostic methods should be supplemented without hesitation by bilateral exploratory trephination *Subdural hematomas* occur most frequently (18 per cent) with a mortality of 36 per cent Next are the *compound fractures* (11 per cent) with a mortality of 31 per cent and permissible sepsis of not over 5 per cent *Depressed fractures* are next (4½ per cent) with a mortality of 5 per cent which should be under 1 per cent and finally the *extradural hematomas* (3 per cent) with a mortality of 55 per cent

Subdural Hemorrhage

This practically always is associated whenever due to a blow on the head with one of the forms of cerebral pathology described in the preceding section The exception occurs in connection with trivial injuries which do not even produce a concussion but which do rupture a bridging vein as it crosses the subdural space Subdural hematomas also develop in the absence of injury and in association with scurvy as an extension from a subarachnoid hemorrhage which originated in cerebral vascular disease or in connection with cerebral tumors and other analogous conditions Except as the end stage of an acute event which follows local injury there are no chronic subdural hematomas The fact that the clot was discovered and treated an appreciable time sometimes years after it had been caused originally by a partly forgotten accident does not justify its segregation into a separate class In a series of over 200 verified subdural hematomas 35 or 11 1 per cent have been present on both sides of the cerebrum and 7 or 3 2 per cent have recurred after operation

Pathology — Subdural hematomas are of three types which merge into one another and vary in their development with the passage of time In their pure form they are either solid mixed or fluid The consistency of any given clot depends upon the original relationship between the solid and fluid elements of the contents of the subdural space They all begin in response to the rupture of a blood vessel and the escape of its contents into that space With all except the solid ones there is an additional tear of the arachnoid and the escape of a varying amount of cerebrospinal fluid into the same subdural space In any case whether made of up a pure solid clot or of a majority of transplanted cerebrospinal fluid to which has been added a minimum of clot or fluid blood the resultant hematoma is incarcerated in its new position and can be removed only by surgery If not so removed the solid clots organize and become either thick walled cysts with small amounts of liquified blood clot in their centre and possible flakes of calcium in their walls or a membraneous sheet of tissue either lying between the arachnoid and dura or added and attached to the latter which thus is thickened locally The mixed and fluid types end up as a collection of fluid with a protein content slightly higher than that of the cerebrospinal fluid They move about freely in the cranial subdural space, shifting with each change in position of the patient s head and remain permanently unabsorbed

The *solid clots* are expansile only during the time of active bleeding Thereafter their effect upon intracranial pressure depends upon their size and the resultant compression of the brain and interference with the ab sorption of the cerebrospinal fluid Their organization takes place only by the extension of fibroblasts from the under side of the dura over both surfaces of the clot As this proceeds an outer membrane next to the dura and an inner membrane next to the arachnoid are formed and sooner or later enclose the entire clot If the clot is small this process of organization from the periphery toward the centre will take place more rapidly than the liquefaction of the enclosed blood This will produce a solid membrane which lies as a sheet beneath the dura or is attached to and an integral part of that structure If the organization is so slow due to the size of the clot that blood in the centre of the hematoma is lique fied a thick walled cyst containing a concentrated solution of protein will result The only further change will be the deposition of calcium in the walls of this cyst The rate of the organization of these solid clots is re markably constant As a result a microscopic study of a section of dura and adjoining membrane and clot will enable one to predict its age and therefore the time of the causative injury with considerable accuracy up to three months As can be appreciated readily this might have con

siderable importance from a medico legal aspect The solid hematomas usually are located over the cerebrum but may occur over the cerebellum

The *mixed clots* being made up of both solid clots and a solution of blood in cerebrospinal fluid are not only expansile during the actual active bleeding but also later by virtue of the protein content of the liquid part This is necessarily high and becomes higher as more and more blood goes into solution The fluid hematoma is separated from the cerebrospinal fluid a solution with a low concentration of protein by the arachnoid The arachnoid acts as a dialyzing membrane and promotes the exchange of fluid and electrolytes from the low to the higher concentrate in accordance with well known physico chemical laws As a result the fluid hematoma constantly is being increased in bulk This increase goes on rapidly until after the free blood has been dissolved and the solid clots have been organized then more slowly until the protein content of the subdural space approximates that of the cerebrospinal fluid The period of rapid expansion reaches its peak about 21 days after the accident and is continued during the following 14 days Thus for about 5 weeks the mixed hematomas are expansile lesions and may be expected to have an increase in intracranial pressure as an accompaniment A static end point in dilution is not reached for another . months but the rate of dilution during this period is so slow and the adjustments of the brain to the widely spread out subdural fluid so adequate that the intracranial pressure remains unchanged at normal Mixed hematomas occur only in the cerebral subdural space and usually as a single collection of fluid which moves freely about the entire space Occasionally there may be two separate fluid collections one on either side of the cerebrum with different chemical contents It has not been determined what the mechanism is that keeps them separate and distinct

Fluid hematomas contain no gross blood clots They originate as a solution of a minimal amount of blood in a maximal amount of cerebrospinal fluid For the reasons given under mixed clots they too are expansile for a period of ten days with a peak on the sixth day Thereafter they are static and their protein content approximates that of cerebrospinal fluid At this time this hematoma and the end stage of the mixed hematoma are indistinguishable The average protein content of these two types of fluid ranges from a high of between 200 and 300 mgm per cent to a low of 75 mgm per cent Suspected fluid that is thought to have been removed from the cerebral subdural space after a cranio cerebral injury and that after being properly analyzed and corrected has a total protein of 100 mgm per cent or over can be classed as subdural fluid Fluids with lower protein however cannot be differ

entiated certainly from subarachnoid fluid on the chemical evidence alone Subdural fluid hematomas whether originally mixed or fluid in type have been shown to be present in the static end stage as long as six years after injury and possibly longer Invariably they have been cerebral in location

Symptoms —The symptoms of the large majority of subdural hematomas are those of the associated brain injury There will be a history of a blow on the head followed by unconsciousness and usually headache as well as all the rest of the variable symptomatology associated with fundamental brain pathology In those few that develop because of the rupture of a bridging vein after a trivial or no known injury to the head there is often but not necessarily always, a late development of symptoms This follows a period of normality which has intervened between the actual rupture and the onset of the patient s complaints In the older cases patients frequently will complain of recurrent waves of symptoms during which they have an indefinite listless type of inertia or lack of initiative and possibly, associated mild headaches and dizzy feelings in the intervals

Signs —The signs are those of whatever associated brain injury may be present A manic type of delusional restlessness is common although stuporous patients tend to become more and more deeply comatose All varieties of reflex changes and peripheral paralyses have been demonstrated Unilateral facial palsy of the central type is an unusually frequent finding Fixed dilation of one pupil usually without demonstrable ptosis of the upper eyelid occurs as frequently on the side opposite to as on the same side as the hematoma The cerebrospinal fluid usually will have the characteristics given it by the associated brain injury Its pressure will be high while the clots are expansile or in the presence of large solid clots but otherwise it will be normal Surgical shock and dehydration will cause lowering of the high pressures but the presence of a subdural hematoma can not be ruled out by the failure to demonstrate a high pressure even in their absence

Diagnosis —Because of the variability and unreliability of the signs and symptoms of all types of subdural hematomas the diagnosis is made finally by a trans temporal exploratory trephinement Ordinarily this should be bilateral It is indicated whenever in acute cases and after surgical shock and dehydration have been ruled out a patient fails to improve or gets worse under properly applied non operative therapy In the older cases it is permissible whenever the patient will consent to undergo the procedure in spite of the expressed assurance of the surgeon that it is quite as likely to prove to be a completely useless therapeutic procedure as it is to be of any help Encephalography and electroenceph

alography will be of assistance only in an insignificant number of solid clots and are entirely useless when the lesion is fluid in type

Treatment — The treatment of all types and ages of subdural hematomas is exclusively operative The preferred technique is by means of a trans temporal procedure Bone flap operations except in the old solid clots and irrigation of the subdural space between trephine holes are contra indicated The clot should be removed completely if fresh and the subdural space drained for 48 hours If old and solid the outer membrane should be opened widely and as much of it and the inner membrane removed as is safe It does no harm to leave large sections of both behind provided the cavity is emptied and drained for 48 hours Specimens of the dura and membranes and of the subdural fluid should be taken invariably and examined histologically and chemically respectively (See also under *Treatment of Edema and Congestion*)

In the less recent cases there is an added element of excessively damaged morale that has to be dealt with These patients have been told so often by so many authorities that their symptoms are either non-existent or hysteroid that they have of necessity become skeptical about assurances of cure no matter who gives them In addition to removing their hematoma and thus relieving them of their symptoms the surgeon has to combat this attitude Furthermore they have in most instances been forced to develop the habit of invalidism This has been their only means of self justification Even with the best intentions and the greatest cooperation this is a hard habit to break Their convalescence is liable to be prolonged and to require much sympathetic assistance on the part of the surgeon

Mortality — The mortality of this group at this time is about 35 per cent This doubtless can be reduced as the diagnoses are made earlier and operative technique becomes more perfect

Compound Fractures of the Skull

Compound fractures of the skull are first of all a problem in sepsis or at least potential sepsis and secondly a problem in the treatment of whatever underlying brain injury is present or whatever complication exists by virtue of the location of the fracture The fracture may be linear comminuted or depressed It may involve venous sinuses or paranasal air sinuses the brain injury may be mild or severe but in any and every instance the case remains one that is at the time or is going to be within 48 hours infected All other considerations of diagnosis and treatment fade into insignificance in the light of this one fact.

Pathology —The pathology is partly that of the fundamental associated brain injury as described in a previous section In addition there is an open infected wound which at the very least involves the outer table of a skull bone and at the very most the subcortical tissue and the blood stream In this wound is a culture medium of bruised necrotic tissue mixed with blood clot and inoculated with or contaminated by bacteria These have been introduced by the compounding agent Foreign bodies such as dirt stones glass bullets pieces of head gear and fragments of bone may be included as well If the fracture line enters the wall of a paranasal air sinus and if the mucous membrane of that sinus is torn in addition there is opened up an extra source for infection of the meninges and brain by direct extension from the nose If the cribriform plate is included the same holds true to a greater degree Thus there is associated with every compound fracture of the skull a potential meningitis encephalitis or cortical abscess If the bacteria that are contaminating the wound are virulent hemolytic streptococci or pneumococci at least meningitis is an actuality from the time of inoculation If the infecting agent belongs to the more common but less virulent staphylococcic group its radial spread beyond the confines of the damaged tissues is less rapid The actual rate of this spread whether measured in distance or time cannot be determined This is because of variables that come from attempting to estimate among other things the degree of blockade of the lymph and blood vessels produced because of mechanical compression from the impact of the compounding agent the virulence of the bacteria the resistance of the patient the manipulation and unintentional massage of the infected tissues during so called cleaning or sterilization procedures and the suitability of the media Experience has demonstrated however that with the exception of cases infected by hemolytic streptococci and pneumococci significant radial spread of bacteria to surrounding previously uninvolved tissues does not take place for 48 hours from the time of implantation *provided the wound is not manipulated* In the later stages foreign bodies besides being harborers of bacteria themselves will produce the tissue changes characteristic of the foreign body reaction ' with its inflammation and even liquefaction with necrosis of adjacent regions

Symptoms and Signs —The symptoms are those of the associated brain lesion The fracture itself produces no symptoms The signs are those characteristic of a lacerated wound of the scalp and underlying tissues including the pericranium This wound will overlie all or part of a fracture line that may be limited to the outer table only or may involve the whole thickness of the bone with comminution or depression of the

fragments In the latter case the meninges may be torn and the surface of the underlying brain lacerated Brain tissue may be lying on the scalp *adjacent to the wound* *There may be bleeding from the nose and mouth* and perhaps a cerebrospinal rhinorrhea if the paranasal air sinuses or the cribriform plate have been included in the fracture line If the compounding has been caused by a bullet it and fragments from it will be visible by x ray *unless it has passed through the cranium* *In this latter case* the compounding will be double In addition any signs that ordinarily might be produced by surgical shock dehydration profuse hemorrhage or any form of brain meningeal or cranial nerve injury will be present *This will include the characteristic cerebrospinal fluid changes*

Diagnosis — The diagnosis can be made accurately only by palpation through the scalp wound with the examiner's sterile finger To do this it is proper to remove previously placed stitches or to enlarge the scalp wound *Adequate time should be taken to be sure of the condition at the first palpation* and thereafter *no further manipulation of the wound by* anyone should be permitted until the surgeon is prepared to follow it up if necessary by a formal debridement Intact pericranium over the fracture line no matter what the condition of the scalp prevents compounding X ray *examination* except to *determine* the *presence* of a *foreign* body such as a bullet or to demonstrate the involvement of the walls of a paranasal sinus in the fracture line is needless and confusing The presence or absence of surgical shock should be ascertained and the degree and type of cerebral injury should be determined by appropriate tests as part of the preoperative diagnosis

Treatment — Once the diagnosis is made therapy is exclusively surgical It consists of debridement with appropriate modifications within 48 hours of the time of the receipt of the accident The physician however has the definite responsibility of seeing to it that no one makes any attempt of any kind to clean or otherwise touch the scalp wound prior to the start of the major surgical procedure The preoperative dressing *should be dry sterile* gauze held *in* place by a bandage and put there immediately after the palpation that has made the diagnosis Specifically no irrigation no shaving of the scalp no removal of dirt or pieces of bone or any similar manipulative procedure should be permitted The importance of this cannot be overestimated Surgical shock and the underlying associated brain pathology should be treated as outlined in a previous section If the preoperative treatment is as outlined the debridement 100 per cent and done sufficiently soon and the fracture does not involve a paranasal sinus the cribriform plate or the supra orbital ridge the operative wound can be closed without drainage and should heal by first in

Pathology — The pathology is partly that of the fundamental associated brain injury as described in a previous section In addition there is an open infected wound which at the very least involves the outer table of a skull bone and at the very most the subcortical tissue and the blood stream In this wound is a culture medium of bruised necrotic tissue mixed with blood clot and inoculated with or contaminated by bacteria These have been introduced by the compounding agent Foreign bodies such as dirt stones glass bullets pieces of head gear and fragments of bone may be included as well If the fracture line enters the wall of a paranasal air sinus and if the mucous membrane of that sinus is torn in addition there is opened up an extra source for infection of the meninges and brain by direct extension from the nose If the cribriform plate is included the same holds true to a greater degree Thus there is associated with every compound fracture of the skull a potential meningitis encephalitis or cortical abscess If the bacteria that are contaminating the wound are virulent hemolytic streptococci or pneumococci at least meningitis is an actuality from the time of inoculation If the infecting agent belongs to the more common but less virulent staphylococcic group its radial spread beyond the confines of the damaged tissues is less rapid The actual rate of this spread whether measured in distance or time cannot be determined This is because of variables that come from attempting to estimate among other things the degree of blockade of the lymph and blood vessels produced because of mechanical compression from the impact of the compounding agent the virulence of the bacteria the resistance of the patient the manipulation and unintentional massage of the infected tissues during so called cleaning or sterilization procedures and the suitability of the media Experience has demonstrated however, that with the exception of cases infected by hemolytic streptococci and pneumococci significant radial spread of bacteria to surrounding previously uninvolved tissues does not take place for 48 hours from the time of implantation *provided the wound is not manipulated* In the later stages foreign bodies besides being harborers of bacteria themselves will produce the tissue changes characteristic of the foreign body reaction with its inflammation and even liquefaction with necrosis of adjacent regions

Symptoms and Signs — The symptoms are those of the associated brain lesion The fracture itself produces no symptoms The signs are those characteristic of a lacerated wound of the scalp and underlying tissues including the pericranium This wound will overlie all or part of a fracture line that may be limited to the outer table only or may involve the whole thickness of the bone with comminution or depression of the

fragments In the latter case the meninges may be torn and the surface of the underlying brain lacerated Brain tissue may be lying on the scalp adjacent to the wound There may be bleeding from the nose and mouth and perhaps a cerebrospinal rhinorrhea if the paranasal air sinuses or the cribriform plate have been included in the fracture line If the compounding has been caused by a bullet it and fragments from it will be visible by x ray unless it has passed through the cranium In this latter case the compounding will be double In addition any signs that ordinarily might be produced by surgical shock dehydration profuse hemorrhage or any form of brain meningeal or cranial nerve injury will be present This will include the characteristic cerebrospinal fluid changes

Diagnosis — The diagnosis can be made accurately only by palpation through the scalp wound with the examiner s sterile finger To do this it is proper to remove previously placed stitches or to enlarge the scalp wound Adequate time should be taken to be sure of the condition at the first palpation and thereafter no further manipulation of the wound by anyone should be permitted until the surgeon is prepared to follow it up if necessary by a formal debridement Intact pericranium over the fracture line *no matter what the condition of the scalp prevents compounding* X ray examination except to determine the presence of a foreign body such as a bullet or to demonstrate the involvement of the walls of a paranasal sinus in the fracture line is needless and confusing The presence or absence of surgical shock should be ascertained and the degree and type of cerebral injury should be determined by appropriate tests as part of the preoperative diagnosis

Treatment — Once the diagnosis is made therapy is exclusively surgical It consists of debridement with appropriate modifications within 48 hours of the time of the receipt of the accident The physician however has the definite responsibility of seeing to it that no one makes any attempt of any kind to clean or otherwise touch the scalp wound prior to the start of the major surgical procedure The preoperative dressing should be dry sterile gauze held in place by a bandage and put there immediately after the palpation that has made the diagnosis Specifically no irrigation no shaving of the scalp no removal of dirt or pieces of bone or any similar manipulative procedure should be permitted The importance of this cannot be overestimated Surgical shock and the underlying associated brain pathology should be treated as outlined in a previous section If the preoperative treatment is as outlined the debridement *100 per cent and done sufficiently soon and the fracture does not involve* a paranasal sinus the cribriform plate or the supra orbital ridge the operative wound can be closed without drainage and should heal by first in

tention Sepsis should not develop in more than 5 per cent of the cases Whenever culture from the wound shows hemolytic streptococci or pneumococci sulphanilamide should be given at once in sufficient quantity to produce and keep a 10 mgm per cent concentration in the blood of the patient Appropriate antipneumococcic serum should be administered also when indicated In all cases of compound fracture into the frontal or ethmoid sinuses or associated with cerebrospinal rhinorrhea the administration of sulphanilamide should be started at once following the admission of the patient to the hospital and without waiting for cultures from the wound or nose Whenever sulphanilamide is used careful daily observations on the white and red blood cell counts should be made to forestall an unexpected development of agranulocytosis or hemolytic anemia Careful observation for other toxic phenomena should be made too (See also under *Treatment of Edema and Congestion*)

Permissible sepsis of any type following compound fracture of the skull should not exceed 5 per cent This probably can be lowered somewhat as soon as the use of sulphanilamide becomes more widespread and better understood The significance of this figure can be appreciated when it is realized that actual analysis of cases of compound fracture of the skull treated by so called general surgical methods shows an incidence of infection of 75 per cent

Mortality — The mortality from compound fracture of the skull should not exceed 25 and should be 20 per cent Widely accepted figures are over 30 and in many instances over 50 per cent

Extradural Hemorrhage

Extradural hematomas have served commonly as the typical prototype of all cranio cerebral injuries This is now known to be entirely incorrect Furthermore it is no longer possible to limit this diagnosis to those cases which have the classical pathognomonic history As a result and since the mortality of these cases rises in direct relationship to the length of time they go undiagnosed it has been necessary to include them in the group of operable cases in whom the final diagnosis may well rest on an exploratory trephination

Pathology — Extradural hematomas practically always are expanding lesions with a constantly growing blood clot which lies between the skull and the dura The source of the clot is found in the rupture of any part of the middle meningeal artery or one of the large cranial venous sinuses The clots commonly are unilateral and cerebral although they may occur simultaneously on both sides of the cerebrum or singly over the cere

bellum They are always associated at the time of the original injury with some one of the forms of fundamental brain pathology

Symptoms — In the classical case the symptoms are pathognomonic The history has three distinct parts Following the blow on the head the patient is knocked unconscious and the artery or sinus ruptured This primary period of unconsciousness is due to the associated fundamental brain pathology and lasts in point of time in accordance with the degree of severity of that pathology If it be only concussion the primary loss of consciousness may be no more than momentary and its presence unknown to the patient or the witnesses and undemonstrable by the physician If it be due to a lacerated brain however the unconsciousness may last for days and extend long past the second stage of the pathognomonic history which is the stage of consciousness Thus the ability to recognize this second period depends on the degree of fundamental brain injury Whether it is recognizable or not however it is during this time that the clot is being formed between the skull and the dura It will be seen that this period must end when the extradural clot is big enough to produce unconsciousness on its own account The length of this second period therefore will depend on the degree of adhesiveness between the dura and the inner surface of the bone If it is slight or absent and the bleeding arterial an enormous clot may be formed in a half hour or less On the other hand if the two structures are firmly attached to one another a clot large enough to deform the cerebrum sufficiently to produce coma may take days to form and may be made up of several successive hemorrhages Regardless of the length of time it lasts however and whether or not its presence is masked completely by the associated cerebral injury this second period is succeeded by a third period of slowly increasing unconsciousness This is due to the coma following *dislocation and compression of the cerebrum by the growing clot It is* recognizable as a third period only if preceded by the typical second period of consciousness This third period ends with the death of the patient if no relief is provided

Signs — All the signs that are present as the result of any type of non operable brain injury may be present in any patient with an extradural hemorrhage In addition during the second period there may be complaint of headache and difficulty with speech During the third period there may be paralysis either ipsi or contra lateral convulsions aphasia possibly a facial palsy dilatation and fixation of one pupil and increased absent or abnormal reflexes X ray data are essential in doubtful cases If the film shows a fracture line which crosses the groove of the middle meningeal artery or a large venous sinus the suspected presence of an

extradural clot will be verified sufficiently to justify operation The film is valueless of course unless both the fracture line and the grooves are visible The intracranial pressure always will be high even in the presence of surgical shock or dehydration The cerebrospinal fluid may or may not be bloody depending on whether there has been an associated contusion or laceration of the brain

Diagnosis — In the classical case the diagnosis is made from the history Such instances are rare In the ordinary case the diagnosis is presumed from the history the physical findings the x ray film and by the failure of the patient to get better under properly applied non operative therapy and is confirmed by prompt transtemporal exploratory trephination

Treatment — This is surgical A sub temporal decompression should be provided at the earliest possible moment the clot completely removed and the bleeding point closed Transfusion for loss of blood almost certainly will prove necessary during and possibly before and after the operation The associated brain injury is treated in accordance with the diagnostic needs The loss of bone in the temporal region is of no consequence provided the attachments of the temporal muscle have been left intact at the time of operation This muscle provides adequate protection against usual injuries (See also under *Treatment of Edema and Congestion*)

Mortality — Extradural hematomas have, in spite of the best and earliest treatment far and away the highest mortality of all cranio cerebral injuries The rate is 55 per cent and is exceeded only by that of complicating meningitis

Depressed Fractures of the Skull

The diagnosis of depressed fracture of the skull should be limited to those cases in which there is no complicating additional scalp bone air sinus or meningeal injury Associated cerebral injury will be present always and may be of any of the non operable varieties

Pathology — The pathology is that of a fracture of one of the bones of the skull which has been in whole or in part moved inward in such a way as to invade the cavity of the cranium It varies from the celluloid ball spoon shaped dent in the infant s skull to the immovable locked fragmented depression of the adult The latter may be linear or comminuted and the fragments may be flat or on edge and may involve both tables or the inner table only Any one of the cranial venous sinuses may be torn by the lacerating fragment as may the dura or the surface of the

brain Old fractures tend to unite in an unreduced position and may produce rounded tumors that stick down into the cranial cavity and make local pressure on the underlying dura and cortex At times however a depressed fracture will heal in such a way as to leave no depression and the inner surface of the bone smooth and flat

Symptoms and Signs — The symptoms are those of the associated brain injury There is usually a sub pericranial or sub-galeal hematoma It is characteristic of the former to develop what appears to be a hard raised edge in relation to the softer centre whether there is a bony depression present or not Diagnosis of this kind of fracture by palpation therefore is notoriously inaccurate The cerebrospinal fluid findings will be those of the associated brain injury X ray usually will demonstrate the depression but occasionally may give a false impression and lead one to diagnose a depression when there is none present or vice versa

Diagnosis — The diagnosis of the bony lesion is made only by x ray The diagnosis of the associated cerebral damage is made as described in the previous sections

Treatment — The treatment is surgical and is carried out by lifting the fragments with as little associated removal of the damaged bone as is consistent with complete elevation All depressed fractures except those in the region of the foramen magnum must be elevated However no elevation should be attempted until after the intracranial pressure has been reduced to and fixed again at a normal level by appropriate therapy of the associated brain injury Because of the cerebral venous congestion it is only in this way that a possible death on the table from operative hemorrhage or air embolus can be avoided If the fracture is not elevated the liability of later convulsive seizures headache and indefinite disabling symptoms is increased (See also under *Treatment of Edema and Congestion*)

Mortality — The mortality rate certainly should not exceed 5 per cent and if the cases are handled properly ought to be zero

Lacerated Wounds Avulsion and Hematomas of the Scalp

Lacerated Wounds of the Scalp — Most such wounds are primarily infected All have an associated galeal hematoma Many contain foreign bodies The treatment therefore is surgical The preferred method is by debridement and primary suture in two layers with interrupted #7 silk stitches and without drainage Next in order of preference is a cleansing with soap and water alcohol ether and 1 per cent alcoholic solution of iodine no suture at all and dressings of gauze soaked in sterile boric oint

ment If stitches are put in they should be loose far apart and through and through drainage with rubber tissue or strands of silk worm gut should be used for 48 hours Flamed adhesive plaster may be used in place of the stitches Under no condition of extent or location should a lacerated wound of the scalp be sewn tightly or without drainage unless an adequate debridement has first been performed properly

Avulsion of the Scalp — The type of treatment suitable for avulsion of the scalp depends primarily upon the blood supply of the avulsed portion All tissue that is viable should be debrided replaced and sutured loosely Dead portions should be sacrificed at once The operation should be done under a general anæsthetic and in a hospital Mechanical antisepsis is used and supplemented by 1 per cent alcoholic solution of iodine A stronger solution cannot be used safely If large areas of bone have been left bare multiple perforations through the outer table into the diploe should be made at once Drainage under the flaps must be provided for 24 hours and multiple scarification of the scalp near all suture lines should be practised Dressings should be kept constantly moist with warm salt solution for 3 or 4 days Skin grafting may be resorted to later if necessary The end results always are much better than the original condition would lead the surgeon to expect

Subperiosteal Hematomas and Cephalhematomas of the New Born — These two types of hematomas of the scalp should be left scrupulously alone if the scalp over them is intact Both of them are completely outside of the bone are limited by the suture lines and will absorb if not infected There is no good evidence to show that their presence causes any intracranial abnormalities

Complications of Cranio Cerebral Injuries

The complications of cranio cerebral injuries fall into four great classes The first covers associated bodily conditions and includes surgical shock and dehydration The second group is made up of conditions that are associated with infection in the cranial cavity The third consists of non specific linear fractures of the base and vault of the skull and lesions caused by them and the fourth covers those conditions that arise as complications out of necessary previous therapy

While the physician must of necessity have a speaking acquaintance with all complications his most intimate association will be with those arising out of general bodily conditions that is surgical shock and dehydration The others may be looked upon as problems in surgical rather than medical therapy and once the physician recognizes their presence and

knows what to expect of surgical therapy he need not concern himself further about them

Complications Due to Associated General Bodily Conditions

Surgical Shock

Surgical shock when present is one of the most important of the complications associated with cranio cerebral injuries It is either an actual or potential accompaniment of all the major ones It differs in no way from the surgical shock that is seen in other major injuries except for an increased preponderance of coma

Pathology —The pathology is in dispute but the best evidence to date is in support of Cannon s theories Briefly according to him a condition is set up in which there is leakage of blood serum or any elec trolyte from the capillaries into the tis ue fluids This reverses the ordi nary osmotic relationships between the intra capillary and extra capillary fluids leads to increased viscosity of the circulating blood an alteration of the relationship between blood cells and serum tissue anoxia and edema decreased systolic and pulse pressure pallor sweating and collapse

Symptoms and Signs —The symptoms of surgical shock include a history of a major injury which if it has been to the head is associated with unconsciousness and on return of consciousne s with moderate disorientation and apprehension The presence of shock usually is char acterized by a falling systolic or persistently low pulse pressure pallor cy anosis sweating subnormal temperature high pulse and rapid respiratory rate If the patient is unconscious often there will be absent reflexes and relaxed sphincters The cerebro pinal fluid pressure except in cases of massive brain injury will be below normal and may be zero The fluid usually is bloody because of the a sociated contusion or laceration of the brain

Diagnosis —The diagnosis hould be made provisionally in the pres ence of any severe cranio cerebral injury and is confirmed by blood pressure pulse and temperature readings and if necessary by the meas urement of the cerebrospinal fluid pressure

Treatment —The best treatment is to administer repeated small trans fusions of properly matched citrated or whole blood One hundred and twenty five to two hundred and fifty c c may be given at each transfu sion There should be also an absolute prohibition of any and all diag nostic or other therapeutic procedures until after the pulse pressure has returned to normal When compatible blood is not available at once and

ment If stitches are put in they should be loose far apart and through and through drainage with rubber tissue or strands of silk worm gut should be used for 48 hours Flamed adhesive plaster may be used in place of the stitches Under no condition of extent or location should a lacerated wound of the scalp be sewn tightly or without drainage unless an adequate debridement has first been performed properly

Avulsion of the Scalp —The type of treatment suitable for avulsion of the scalp depends primarily upon the blood supply of the avulsed portion All tissue that is viable should be debrided replaced and sutured loosely Dead portions should be sacrificed at once The operation should be done under a general anesthetic and in a hospital Mechanical antisepsis is used and supplemented by 1 per cent alcoholic solution of iodine A stronger solution cannot be used safely If large areas of bone have been left bare multiple perforations through the outer table into the diploe should be made at once Drainage under the flaps must be provided for 24 hours and multiple scarification of the scalp near all suture lines should be practised Dressings should be kept constantly moist with warm salt solution for 3 or 4 days Skin grafting may be resorted to later if necessary The end results always are much better than the original condition would lead the surgeon to expect

Subperiosteal Hematomas and Cephalhematomas of the New Born — These two types of hematomas of the scalp should be left scrupulously alone if the scalp over them is intact Both of them are completely outside of the bone are limited by the suture lines and will absorb if not infected There is no good evidence to show that their presence causes any intracranial abnormalities

Complications of Cranio Cerebral Injuries

The complications of cranio cerebral injuries fall into four great classes The first covers associated bodily conditions and includes surgical shock and dehydration The second group is made up of conditions that are associated with infection in the cranial cavity The third consists of non specific linear fractures of the base and vault of the skull and lesions caused by them and the fourth covers those conditions that arise as complications out of necessary previous therapy

While the physician must of necessity have a speaking acquaintance with all complications his most intimate association will be with those arising out of general bodily conditions that is surgical shock and dehydration The others may be looked upon as problems in surgical rather than medical therapy and once the physician recognizes their presence and

knows what to expect of surgical therapy he need not concern himself further about them

Complications Due to Associated General Bodily Conditions

Surgical Shock

Surgical shock when present is one of the most important of the complications associated with cranio cerebral injuries It is either an actual or potential accompaniment of all the major ones It differs in no way from the surgical shock that is seen in other major injuries except for an increased preponderance of coma

Pathology —The pathology is in dispute but the best evidence to date is in support of Cannon s theories Briefly according to him a condition is set up in which there is leakage of blood serum or any electrolyte from the capillaries into the tissue fluids This reverses the ordinary osmotic relationships between the intra capillary and extra capillary fluid leads to increased viscosity of the circulating blood an alteration of the relationship between blood cells and serum tissue anoxia and edema decreased systolic and pulse pressure pallor sweating and collapse

Symptoms and Signs —The symptoms of surgical shock include a history of a major injury which if it has been to the head is associated with unconsciousness and on return of consciousness with moderate disorientation and apprehension The presence of shock usually is characterized by a falling systolic or persistently low pulse pressure pallor cyanosis sweating subnormal temperature high pulse and rapid respiratory rate If the patient is unconscious often there will be absent reflexes and relaxed sphincters The cerebrospinal fluid pressure except in cases of massive brain injury will be below normal and may be zero The fluid usually is bloody because of the associated contusion or laceration of the brain

Diagnosis —The diagnosis should be made provisionally in the presence of any severe cranio cerebral injury and is confirmed by blood pressure pulse and temperature readings and if necessary by the measurement of the cerebrospinal fluid pressure

Treatment —The best treatment is to administer repeated small transfusions of properly matched citrated or whole blood One hundred and twenty five to two hundred and fifty c c may be given at each transfusion There should be also an absolute prohibition of any and all diagnostic or other therapeutic procedures until after the pulse pressure has returned to normal When compatible blood is not available at once and

it usually is not a 50 per cent solution of glucose if given intravenously in doses of 100 c c at a time for adults is a satisfactory substitute until a donor can be obtained An even more satisfactory substitute is a solution of pure acacia This however generally is not available in a form that can be safely used in an emergency Normal salt solution and adrenalin are contra indicated as methods of treatment for surgical shock The first, being a solution of electrolytes leaks from the capillaries almost as fast as it is put into the circulating blood and thus increases tissue anoxemia and edema The second increases the resistance of the peripheral circulation and thus reduces still further the already inadequate supply of oxygen bearing blood to the cells and as a result tissue anoxemia and cellular damage are increased Solutions of glucose and acacia are useful because the large size of their molecule retards their escape from the leaky capillaries and they can thus serve to increase the volume of circulating blood Normal blood is useful because it provides a mechanism whereby the oxygen carrying capacity as well as the volume of the circulating blood is increased Phenolbarbital (luminal) by mouth in small doses and caffeine sodium benzoate intravenously may be of aid In addition the customary general therapeutic measures must be used

No figures are available as to the rates of occurrence or mortality

Toxic Dehydration

Toxic dehydration is one of the commonest but most universally unrecognized complications of cranio cerebral injuries There is no test which will demonstrate accurately its presence or absence and the diagnosis has to be made on clinical evidence only

Pathology —The pathology is that associated with an imbalance of the water metabolism of the body Acidosis may be present in severe cases

Symptoms and Signs —There is a history of a blow on the head and a period of unconsciousness either from 3 to 4 or from 10 to 14 days previously If the patient has regained consciousness previously there is increasing stupor In the variety that develops early usually there has been vomiting profuse sweating overheating from any cause and an intentional or accidental limitation of fluid intake especially in unconscious patients Thus the latter has been associated with a major but unnoticed and uncompensated fluid loss In the late variety the history usually will reveal an over-dosage of either hypertonic solutions intravenously or of magnesium sulphate solution by rectum Their original use may have had a therapeutic justification but that no longer exists Often there will be a history of ether or barbiturate anesthesia and possibly an operation is

a starting point Both types usually will show a rising temperature a major discrepancy between the amounts of fluid intake and output as charted graphically a subnormal intracranial pressure which may be zero and in the more serious instances acetonuria and a decrease in the carbon dioxide combining power of the blood The latter is particularly apt to develop in young children from what would appear to be inadequate reasons

Treatment — Treatment consists of the administration at all times of sufficient fluid to prevent dehydration In adults this requires under ordinary circumstances the ingestion or absorption into the body by other means of at least 3 500 c c for each 24 hour period If toxic dehydration develops this fluid intake must be stepped up to between 5 000 and 6 000 c c in each 24 hour period Appropriate adjustments in intake must be made in children chronic cardiacs and in patients that develop edema of the extremities or lungs from any cause Fluid is given preferably by mouth but can be given by hypodermoclysis or through an inlying stomach tube

Ratio of Occurrence — This condition occurs in about 2 6 per cent of hospitalized patients with cranio-cerebral injuries

Mortality — It is not necessarily a serious or fatal complication but it may prove to be so if unrecognized or if allowed to progress without treatment The mortality among hospitalized patients is 20 per cent

Complications Due to Infection in the Cranium and Cranial Cavity

Regardless of the type of treatment used a certain amount of infection is inevitable in any significant group of surgical cases In cranio-cerebral injuries it commonly takes the form of meningitis brain abscess osteomyelitis or an infected scalp wound The incidence of infection in a hospitalized group of over 1 200 such cases whether of the operable or non operable type was about 3 per cent and the mortality 51 per cent Two and one tenth per cent of this infection was considered to be unjustifiable Practically all of these latter followed operative interference Of the remaining 0 9 per cent a little more than half were in the non operable group

Meningitis

Meningitis in association with a cranio-cerebral injury most commonly is caused by the staphylococcus next by the streptococcus and less often by the pneumococcus and influenza bacillus

Pathology — The pathology is classical and differs in no way from that seen in the absence of cranial injury

Symptoms and Signs — The symptoms like the pathology are classical also They include high fever, delirium or stupor stiff neck headache incontinence and so forth In the non operable group of these injuries a fracture of the temporal bone the cribriform plate or into the cavity of one of the paranasal air sinuses usually can be demonstrated as the source of the infection In the operable group the source practically invariably is found in the wound There are the usual signs to be elicited by neurological examination The cerebrospinal fluid will be under a high pressure there will be pleiocytosis and the total protein content will be elevated If bacteria are present a drop in the cerebrospinal fluid sugar and chloride content will be a constant finding On the other hand a rise will be a favorable prognostic sign and usually will coincide with clinical improvement Cultures may or may not be positive

Diagnosis — The diagnosis is made from the cerebrospinal fluid findings The infecting organism may be identified by cultures taken from the cerebrospinal fluid the blood stream the nasal cavity or the operative wound

Treatment — This is notoriously, but not invariably unsuccessful The use of sulphanilamide in initial and maintenance doses sufficient to maintain a concentration of 10 mgm per cent of drug in the blood stream is very effective for hemolytic streptococcal and pneumococcal infections Alkalis should be administered by mouth to prevent acidosis and care should be taken to forestall the development of anemia by giving blood transfusions when indicated The administration of the drug should be discontinued when the white blood cell count begins to drop to avoid the danger of agranulocytosis or if other severe toxic manifestations appear Appropriate anti pneumococcic serum should be used in combination with sulphanilamide in the treatment of pneumococcic meningitis There is also some reason to believe that in larger doses it may be effective against influenzal bacillus meningitis For the latter there is available a specific anti serum In all these infections and in the staphylococcic as well older therapeutic methods should not be neglected however Not a few such cases of meningitis were cured before the advent of sulphanilamide by a combination of extreme hydration and lumbar drainage every 4 hours To do this fluids must be forced to the point of 6 000 c c every 24 hours and the lumbar sac drained dry of cerebrospinal fluid every 4 hours day and night Tidal drainage to care for incontinence transfusions for anemia and high caloric high vitamin diets all are essential adjuncts Such therapy must be continued until the sugar chloride protein and

cellular content of the cerebrospinal fluid have become fixed at normal regardless of earlier symptomatic improvement The administration of serum intra thecally should be avoided as its presence there is apt to cause the development of a subarachnoid block and thus prevent drainage of the cerebral spaces by a lumbar tap

Ratio of Occurrence — In the non operable types of hospitalized cranio cerebral injuries meningitis occurs in about ¼ of 1 per cent of the cases

Mortality — Before the advent of sulphanilamide the mortality was above 80 and below 100 per cent It has doubtless improved since but the figures are not yet available

Brain Abscess

This is a strictly surgical and an extremely complicated problem and can only be touched on briefly here It is discussed also in Vol VI Chapt IV

Pathology — Brain abscesses are of two types The commonest is the encapsulated This type of abscess may be either single or multiple usually only single in cranio cerebral injuries cerebral or cerebellar and subcortical cortical and sub or extra dural The abscess consists of a collection of infected necrotic material contained within a relatively thick walled capsule It may increase in size and rupture into the ventricular or meningeal spaces and cause meningitis It may become sterile and be absorbed or calcified or remain as a sterile cyst The second type is the encephalitic This in cranio-cerebral injuries usually is the result of a direct spread of infection from the cranium or scalp It has no capsule spreads by radial infected thrombi and shortly produces meningitis or ventriculitis It is most commonly seen otherwise as a metastasis from some distant source of infection

Symptoms and Signs — The symptoms and signs of both types are those of an expanding intracranial lesion with or without evidence of an infection in the cranium or scalp Although there is usually a moderate cerebrospinal pleiocytosis this is by no means invariable The chemistry usually is normal except for a possible moderate increase in total protein The intracranial pressure usually is high but may not be greatly elevated

Diagnosis — The diagnosis may be extremely difficult frequently has to be made with the aid of ventriculography or encephalography and is usually confirmed only by exploratory needling of the suspected areas of the brain

Treatment — Treatment is exclusively surgical and predicates drainage of the abscess preferably either by the insertion under the eye of the Mosher copper wire cone drain or induced extravasation after the method

Pathology — The pathology is classical and differs in no way from that seen in the absence of cranial injury

Symptoms and Signs — The symptoms like the pathology are classical also They include high fever delirium or stupor stiff neck headache incontinence and so forth In the non operable group of these injuries a fracture of the temporal bone the cribriform plate or into the cavity of one of the paranasal air sinuses usually can be demonstrated as the source of the infection In the operable group the source practically invariably is found in the wound There are the usual signs to be elicited by neurological examination The cerebrospinal fluid will be under a high pressure there will be pleiocytosis and the total protein content will be elevated If bacteria are present a drop in the cerebrospinal fluid sugar and chloride content will be a constant finding On the other hand a rise will be a favorable prognostic sign and usually will coincide with clinical improvement Cultures may or may not be positive

Diagnosis — The diagnosis is made from the cerebrospinal fluid findings The infecting organism may be identified by cultures taken from the cerebrospinal fluid the blood stream the nasal cavity or the operative wound

Treatment — This is notoriously but not invariably unsuccessful The use of sulphanilamide in initial and maintenance doses sufficient to maintain a concentration of 10 mgm per cent of drug in the blood stream is very effective for hemolytic streptococcal and pneumococcal infections Alkalis should be administered by mouth to prevent acidosis and care should be taken to forestall the development of anemia by giving blood transfusions when indicated The administration of the drug should be discontinued when the white blood cell count begins to drop to avoid the danger of agranulocytosis or if other severe toxic manifestations appear Appropriate anti pneumococcic serum should be used in combination with sulphanilamide in the treatment of pneumococcic meningitis There is also some reason to believe that in larger doses it may be effective against influenzal bacillus meningitis For the latter there is available a specific anti serum In all these infections and in the staphylococcic as well older therapeutic methods should not be neglected however Not a few such cases of meningitis were cured before the advent of sulphanilamide by a combination of extreme hydration and lumbar drainage every 4 hours To do this fluids must be forced to the point of 6 000 c c every 24 hours and the lumbar sac drained dry of cerebrospinal fluid every 4 hours day and night Tidal drainage to care for incontinence transfusions for anemia and high caloric high vitamin diets all are essential adjuncts Such therapy must be continued until the sugar chloride protein and

hand the appearance of normal venous markings may lead to a diagnosis of fracture when there actually is none

Treatment — Simple linear and comminuted fractures of the skull of themselves call for no treatment

Ratio of Occurrence — This is not known

Mortality — There is none

Injuries Other Than Those of the Cerebrum Cerebellum and Meninges that are Associated with simple Fractures

If properly placed simple linear or comminuted fractures may damage certain of the cranial nerves and blood vessels The nerves are commonly the optic any of the oculomotor nerves the trigeminal and the facial

Diagnosis — The diagnosis is obvious in every case as soon as the physician demonstrates the motor or sensory palsy that necessarily is associated with the nerve injury Particular care should be taken however to recognize blindness loss of corneal sensibility and paralysis of the orbicularis palpebrarum and frontalis muscles Whenever there is a partial or complete division of the optic nerve the patient or his legal representative should be notified at once Only in this way can the doctor surely protect himself against later claims that the loss of vision is due to his treatment or lack of it This is particularly important if the patient is comatose or uncooperative and as a result fails to recognize his disability until after a relatively long period of time If the division of the nerve has been complete and provided there has been no interruption of the retinal blood supply there will be a loss of the light reflex and after a suitable interval the ophthalmoscopic signs of secondary optic atrophy Loss of corneal sensibility from fifth nerve injury and inability to close the eye from facial nerve injury if not recognized early may lead to corneal scars and interference later with vision because of them

Treatment — There is no effective treatment for a division of the optic nerve or the resultant blindness Corneal scars can be prevented in most cases by the application of an air tight goggle or similar covering to the affected eye This produces a moist chamber and prevents direct or indirect damage to the corneal epithelium In severe cases the lids can be sutured Suitable goggles can be obtained from many stores or may be made of individually shaped celluloid on a spectacle frame In the facial nerve cases electrical stimulation of the paralyzed muscles daily massage of the face from the corner of the mouth upward toward the external auditory meatus and finally implantation of subcutaneous fascial or muscle slings should all be used as part of the local therapy

of J E J King Its rate of occurrence among cranio-cerebral injuries and its mortality are not known The liability of these cases to late symptoms however must be high on account of the associated cortical scars

Osteomyelitis and Infected Scalp Wounds

These are characteristic of a relatively benign infection of the cranial bones or of the scalp There is a tendency to abscess formation locally The infection almost never spreads through the diploe A similar type of osteomyelitis sometimes occurs in children in connection with furunculosis of the scalp and in the absence of trauma

Symptoms and Signs — They are those of a persistently draining wound with bare dead bone frequently palpable in its depths

Diagnosis — This is made from the classical signs of local inflammation and either with or without the help of the x ray

Treatment — This includes excision of the dead bone and drainage of the infection and is always surgical

Ratio of Occurrence and Mortality — These figures are not available

Simple and Complicating Fractures of the Vault and Base of the Skull other than Compound or Depressed Fractures

Simple Linear or Comminuted Fractures

Simple linear or comminuted fractures probably are the commonest associate of cranio cerebral injuries They are still made to serve as the focal point of medicolegal interest in these cases and the medical profession still persists in the useless differentiation between those of the base and those of the vault They are distinguishable from complicating linear and comminuted fractures by the fact that they do not involve the accessory paranasal sinuses and the cavities of the nose ear and mastoid Their presence has no significance other than to serve as evidence that the bone containing the fracture came in contact with some stationary or moving object Their importance lies in the damage they cause to vessels and nerves which have been in direct contact with them at the time of their formation

Diagnosis — The diagnosis of a linear or comminuted fracture is made by x ray It should not be forgotten however that the x ray films are not necessarily 100 per cent correct and that the coincidence of adjacent shadows the angle of the ray and the like may on the one hand prevent visualization of fracture lines that are actually present while on the other

hand the appearance of normal venous markings may lead to a diagnosis of fracture when there actually is none

Treatment — Simple linear and comminuted fractures of the skull of themselves call for no treatment

Ratio of Occurrence — This is not known

Mortality — There is none

Injuries Other Than Those of the Cerebrum Cerebellum and Meninges that are Associated with simple Fractures

If properly placed simple linear or comminuted fractures may damage certain of the cranial nerves and blood vessels The nerves are commonly the optic any of the oculomotor nerves the trigeminal and the facial

Diagnosis — The diagnosis is obvious in every case as soon as the physician demonstrates the motor or sensory palsy that necessarily is associated with the nerve injury Particular care should be taken however to recognize blindness loss of corneal sensibility and paralysis of the orbicularis palpebrarum and frontalis muscles Whenever there is a partial or complete division of the optic nerve the patient or his legal representative should be notified at once Only in this way can the doctor surely protect himself against later claims that the loss of vision is due to his treatment or lack of it This is particularly important if the patient is comatose or uncooperative and as a result fails to recognize his disability until after a relatively long period of time If the division of the nerve has been complete and provided there has been no interruption of the retinal blood supply there will be a loss of the light reflex and after a suitable interval the ophthalmoscopic signs of secondary optic atrophy Loss of corneal sensibility from fifth nerve injury and inability to close the eye from facial nerve injury if not recognized early may lead to corneal scars and interference later with vision because of them

Treatment — There is no effective treatment for a division of the optic nerve or the resultant blindness Corneal scars can be prevented in most cases by the application of an air tight goggle or similar covering to the affected eye This produces a moist chamber and prevents direct or indirect damage to the corneal epithelium In severe cases the lids can be sutured Suitable goggles can be obtained from many stores or may be made of individually shaped celluloid on a spectacle frame In the facial nerve cases electrical stimulation of the paralyzed muscles daily massage of the face from the corner of the mouth upward toward the external auditory meatus and finally implantation of subcutaneous fascial or muscle slings should all be used as part of the local therapy

If the optic nerve is severed the blindness is complete and permanent The oculomotor the fifth and facial nerves may all be interrupted only physiologically although the symptoms be those of an anatomical division In such cases provided adequate temporary care of the muscles and of the eye ball is taken until conduction is again resumed later disability will be nil Furthermore since such injuries to these nerves occur to their post ganglionic portion even complete anatomical division need not predicate permanent loss of function providing their peripheral supply is kept in order until regrowth of the axones can take place This process may in certain cases be expedited by suture decompression or anastamosis The end results therefore will depend in part on the care of their peripheral supply and in part on the success of the artificial reparative processes that are resorted to to promote regrowth or replacement of the destroyed axones

Ratio of Occurrence — This is not known

Mortality — There is no mortality

Traumatic Arterio Venous Aneurysm

For practical purposes the only blood vessel within the cranium that is injured in association with uncomplicated linear or comminuted fractures of the skull is the internal carotid artery Others such as the venous sinuses and the middle meningeal arteries when injured produce syndromes that are of sufficient importance to justify segregation as extra or sub-dural hematomas A fracture in the middle fossa involving the body of the sphenoid bone may either rupture the wall of the carotid artery at the time or damage it sufficiently so that it will break a few days later Because of the anatomical relationships the part of the artery that is injured is that which lies within and surrounded by the cavernous sinus Thus arterial blood is introduced into a large vein and since the collection of this venous blood normally is from the contents of the orbit such an arterio venous aneurysm produces a pulsating exophthalmos

Symptoms and Signs — The symptoms are associated chiefly with a constant roaring in the patient s head the development of which may follow within a few hours of or some days after a blow on the skull A bruit can be heard through a stethoscope applied over the affected eye and often over a large adjacent area of skull There will be a slowly developing pulsating exophthalmos with all the eye signs associated with either a mild or severe degree of protrusion of the eyeball There may be varying degrees of extra-ocular muscular palsy X ray examination usually is negative and there need not be any severe associated brain injury

The bruit and symptoms will be improved or done away with if the common or internal carotid artery is closed by pressure on the neck

Diagnosis — The diagnosis is made on the history of the subjective intracranial roaring the exophthalmos and the temporary relief of symptom following closure of the involved carotid artery

Treatment — The treatment may be only palliative at best It is more likely to be effective if instituted very early and if the break in the arterial wall is minimal Therapy is both possible and relatively ineffective because of the anastamoses through the circle of Willis It is accomplished by the permanent closure of the internal or common carotid artery in the neck Before this can be done without undue risk of hemiplegia or death the collateral circulation must be stimulated and increased locally This can be done best by the patient himself and should be started at the earliest possible moment He compresses his common carotid artery against the cervical spine in such a way as to close it completely The artery should be held closed until the patient begins to feel faint The length of time of closure thus will increase automatically and when it reaches 30 minutes without the production of any subjective symptoms permanent operative closure can be undertaken The preliminary procedure usually requires about seven weeks The operation is done best in two stages In the first the common carotid artery is exposed in the neck and closed by the application of a Matas aluminum band Two weeks or more later the internal carotid artery is exposed through the same or a higher incision and also closed by the same method These wounds must be completely aseptic and should be drained for at least 24 hours but no longer Hemostasis must be most meticulous A spreading thrombosis which gradually fills the carotid tree on the operated side is a possible but unpredictable result of such an artificial occlusion Death necessarily ensues if this happens

Complicating Fractures of the Skull

Complicating fractures of the skull are those linear or comminuted fractures that are neither depressed nor compounded and that involve in their course the paranasal air sinuses the cribriform plate and the cavities of the nose ear and mastoid

Fractures of Temporal Bone

The most common are the fractures of the temporal bone which extend into some part of the ear either with or without involvement of the mastoid

If the optic nerve is severed the blindness is complete and permanent The oculomotor the fifth and facial nerves may all be interrupted only physiologically although the symptoms be those of an anatomical division In such cases provided adequate temporary care of the muscles and of the eye ball is taken until conduction is again resumed later disability will be nil Furthermore since such injuries to these nerves occur to their post ganglionic portion even complete anatomical division need not predicate permanent loss of function providing their peripheral supply is kept in order until regrowth of the axones can take place This process may in certain cases be expedited by suture decompression or anastamosis The end results therefore will depend in part on the care of their peripheral supply and in part on the success of the artificial reparative processes that are resorted to to promote regrowth or replacement of the destroyed axones

Ratio of Occurrence — This is not known

Mortality — There is no mortality

Traumatic Arterio Venous Aneurysm

For practical purposes the only blood vessel within the cranium that is injured in association with uncomplicated linear or comminuted fractures of the skull is the internal carotid artery Others such as the venous sinuses and the middle meningeal arteries when injured produce syndromes that are of sufficient importance to justify segregation as extra or sub dural hematomas A fracture in the middle fossa involving the body of the sphenoid bone may either rupture the wall of the carotid artery at the time or damage it sufficiently so that it will break a few days later Because of the anatomical relationships the part of the artery that is injured is that which lies within and surrounded by the cavernous sinus Thus arterial blood is introduced into a large vein and since the collection of this venous blood normally is from the contents of the orbit such an arterio venous aneurysm produces a pulsating exophthalmos

Symptoms and Signs — The symptoms are associated chiefly with a constant roaring in the patient s head the development of which may follow within a few hours of or some days after a blow on the skull A bruit can be heard through a stethoscope applied over the affected eye and often over a large adjacent area of skull There will be a slowly developing pulsating exophthalmos with all the eye signs associated with either a mild or severe degree of protrusion of the eyeball There may be varying degrees of extra-ocular muscular palsy X ray examination usually is negative and there need not be any severe associated brain injury

of non traumatic Menière s syndrome methods looking toward completing the destruction of the already partially destroyed and damaged labyrinth have been advised and used The most successful is that surgical procedure in which the vestibular part of the eighth nerve on the affected side is divided in the posterior fossa of the skull In this way a certain functional destruction of the damaged labyrinth is assured and there is no interference with the hearing of the ear in question Complete relief of symptoms may be expected in these traumatic Menière s cases in about 85 per cent of the patients as contrasted with the 100 per cent relief attained by the same therapy in the non traumatic group

Ratio of Occurrence and Mortality It has proved impossible to collect these figures with any degree of accuracy

Fractures Involving Cribriform Plate or Paranasal Sinuses

Fractures involving the cribriform plate or paranasal sinuses while less common are much more serious

Pathology — In either case communication with the nose is established and the local pathological picture is characteristic of and depends upon the upward spread of infection from the nasal cavities

Diagnosis — The diagnosis is made by x ray by the escape of the cerebrospinal fluid from the nose with or without blood or by the demonstration of air inside the skull By far the most dangerous cases are those with the cerebrospinal fluid rhinorrhea

Treatment — The chances of treating this condition successfully by repeated lumbar punctures are extremely remote Yet if it is not stopped promptly meningitis is an inevitable certainty An early operative exposure of the fracture and upper end of the fistulous tract followed by plastic closure of the dural tear is essential This should be undertaken as soon as the patient s condition warrants and with a full appreciation of its magnitude

Fracture of Posterior Wall of Frontal Sinus

Fracture of the posterior wall of the frontal sinus is a not infrequent form of fracture of the skull with the compounding into the nasal cavities rather than through the scalp The *diagnosis* is made by x ray

Treatment — There is no one rule for treating these cases Each is an individual problem and treatment in the last analysis depends upon whether or not the surgeon believes that the mucous membrane lining of the sinus is torn If he does the sinus should be entered surgically the

Pathology — Their presence permits communication between the sterile meningeal spaces and the possibly infected ear or mastoid cavities Some degree of brain injury always is associated with them

Symptoms and Signs — The symptoms include dizziness unsteadiness nystagmus loss of hearing facial palsy and loss of the sense of taste Any one may be either transitory or permanent This communication between the meninges and the ear is certain if cerebrospinal fluid escapes from the ear and is probable if there is any amount of bleeding from the same source There may be associated damage to the seventh and eighth cranial nerves the drum or the labyrinth Meningitis by direct extension is a possibility at any time up to 2 weeks after the injury

Diagnosis — The diagnosis is made most surely by the demonstration of cerebrospinal fluid flowing from the external auditory meatus Other signs are those provided by means of x ray films by a hematoma over the mastoid or a fracture line visible through the otoscope in the middle or inner ear Acute traumatic labyrinthitis from labyrinthine hemorrhage and associated with deafness may by the Barany or caloric irrigation tests show either hypo or hyper activity of the damaged labyrinth

Treatment — The treatment is to avoid all manipulation of the ear and especially to avoid plugging or irrigating the canal If there is an escape of cerebrospinal fluid it is necessary to keep the intracranial pressure low by early and frequent lumbar punctures This permits collapse of the subarachnoid space adjacent to the meningeal tear and favors healing of the arachnoid membrane

When disabling labyrinthine symptoms have been present and unabated for a year or more it is probable that they will be permanent Any relief from the unsteadiness and vertigo will come only from the patient s ability to adjust himself to the new conditions under which he is forced to live unless he can get help from some surgical procedure If his intellectual level is high and his morale good this latter may not be necessary but if adjustments cannot be made its adoption may well prove indispensable The degree of neurosis of lowering of the morale and of the tendency to live a more and more secluded and antisocial life will be the factors that determine the future treatment These cases fall within the group that is covered by the diagnosis *Traumatic Aural Vertigo* or *Traumatic Ménière s Syndrome* Successful treatment of this chronic disabling lesion depends upon the recent demonstration that one s sense of position in space is normal only when either the integration and joint action of both labyrinths is perfect or when the control is vested in one labyrinth alone the other being completely dead From this premise and more recently because of the increasing success of the operative treatment

shaped scar in the scalp and temporal muscle usually is adherent to the underlying cortex or arachnoid or both The e and the soft tissues of the scalp all are fused into one fibrous mass at the periphery of the defect and in turn are firmly adherent to its edge of bone

Symptoms and Signs — The chief symptom is a feeling of looseness of the brain inside the skull so that the brain rattles' This creates a marked sense of insecurity The pulsation of the scalp in the region of the defects is another equally constant but less disturbing symptom There are no significant signs in the defects themselves other than the scalp scar the constant pulsation and the filling and emptying of the defect with every change of position of the patient s head

Treatment — The treatment is operative The essential steps are to create new edges of bone and dura separate all adhesions to the cortex and fill the dural defect with a free transplant of fascia lata The bony defect in this area need not be filled Usually it is only necessary to close one side in order to relieve the symptoms Both sides can however be repaired should it prove necessary

Post operative Defects in the Skull Bones

For the most part artificially produced cranial defects following treatment of cranio cerebral injuries are small Their repair usually is only necessary for esthetic reasons and is therefore most liable to be required for those defects that lie outside of the hair line Among those that are within the hair line repair is required only for the larger ones and only then if they overlie the motor cortex The large majority have been at the least the site of drainage and usually have been infected as well For that reason their repair always must be postponed until such time as the surgeon can be reasonably sure that his operation will not stir up a residual quiescent infection that otherwise would not become activated Such a mishap will lead to the extrusion and loss of the transplant and may even be directly followed by meningitis or other major intracranial infection It should be assumed until disproven that all bone defects are associated with underlying defects in the dura as well as being the site of widespread adhesions between that membrane the bone edge the cortex and the scalp Essential parts of every reparative operation are those which free all these adhesions and close the dural defect by a transplant of fascia lata If the bony deficiency is filled without these added steps the strong probability is that there will be no subsequent relief of the patient s symptoms

Bony defects that require filling are either *supra orbital* or *parieto*

membrane removed the posterior wall excised and the sinus cavity and epidural space drained If he does not there need be no operative interference There is no certain way of determining the presence of such a tear except by demonstrating air either in or outside of the meninges Even then if the patient is improving steadily operative interference will be neither necessary nor wise If symptoms persist or increase or signs of meningeal irritation arise operation is imperative It is probable that the great majority of these fractures are asymptomatic The occurrence of meningitis has been given in one series as 0 8 per cent

Mortality and Ratio of Occurrence — These figures are not available

Aerocele

The abnormal presence of air in the skull is extremely rare and usually associated with a fracture of one frontal sinus The air may not appear for some days and then only after a sneeze or an attempt by the patient to blow his nose Its presence indicates a communication between the nose and the meninges and as such in all probability calls for operative interference

Complications Due to Necessary Treatment

Because of their severity and situation many cranio cerebral injuries require emergency treatment This must be provided regardless of whether or not it creates a situation that later and in its turn requires further therapy At this later date the original injury has long since healed and although originally arising as a complication of the former the later condition will be an entity in itself and have its own signs symptoms and pathology and require its own specialized therapy Necessary treatment for this type of complication invariably is surgical

Bilateral Subtemporal Decompression

As the result of necessary operative procedures patients who have sustained cranio cerebral injuries are left at times with bilateral temporal bony defects If both are of any significant size late closure of at least one may prove to be essential to the patient s final and complete recovery

Pathology — There is an absence of a part of the squamous temporal and often adjoining portions of the frontal and parietal bones on both sides of the skull The bone defects overlie defects in the dura which are of approximately the same size The vertical or inverted horseshoe

shaped scar in the scalp and temporal muscle usually is adherent to the underlying cortex or arachnoid or both These and the soft tissues of the scalp all are fused into one fibrous mass at the periphery of the defect and in turn are firmly adherent to its edge of bone

Symptoms and Signs —The chief symptom is a feeling of looseness of the brain inside the skull so that the brain rattles This creates a marked sense of insecurity The pulsation of the scalp in the region of the defects is another equally constant but less disturbing symptom There are no significant signs in the defects themselves other than the scalp scar the constant pulsation and the filling and emptying of the defect with every change of position of the patient s head

Treatment —The treatment is operative The essential steps are to create new edges of bone and dura separate all adhesions to the cortex and fill the dural defect with a free transplant of fascia lata The bony defect in this area need not be filled Usually it is only necessary to close one side in order to relieve the symptoms Both sides can however be repaired should it prove necessary

Post operative Defects in the Skull Bones

For the most part artificially produced cranial defects following treatment of cranio-cerebral injuries are small Their repair usually is only necessary for esthetic reasons and is therefore most liable to be required for those defects that lie outside of the hair line Among those that are within the hair line repair is required only for the larger ones and only then if they overlie the motor cortex The large majority have been at the least the site of drainage and usually have been infected as well For that reason their repair always must be postponed until such time as the surgeon can be reasonably sure that his operation will not stir up a residual quiescent infection that otherwise would not become activated Such a mishap will lead to the extrusion and loss of the transplant and may even be directly followed by meningitis or other major intracranial infection It should be assumed until disproven that all bone defects are associated with underlying defects in the dura as well as being the site of widespread adhesions between that membrane the bone edge the cortex and the scalp Essential parts of every reparative operation are those which free all these adhesions and close the dural defect by a transplant of fascia lata If the bony deficiency is filled without these added steps the strong probability is that there will be no subsequent relief of the patient s symptoms

Bony defects that require filling are either *supra orbital* or *parieto*

membrane removed the posterior wall excised and the sinus cavity and epidural space drained If he does not there need be no operative interference There is no certain way of determining the presence of such a tear except by demonstrating air either in or outside of the meninges Even then if the patient is improving steadily operative interference will be neither necessary nor wise If symptoms persist or increase or signs of meningeal irritation arise operation is imperative It is probable that the great majority of these fractures are asymptomatic The occurrence of meningitis has been given in one series as 0 8 per cent

Mortality and Ratio of Occurrence — These figures are not available

Aerocele

The abnormal presence of air in the skull is extremely rare and usually associated with a fracture of one frontal sinus The air may not appear for some days and then only after a sneeze or an attempt by the patient to blow his nose Its presence indicates a communication between the nose and the meninges and as such in all probability calls for operative interference

Complications Due to Necessary Treatment

Because of their severity and situation many cranio-cerebral injuries require emergency treatment This must be provided regardless of whether or not it creates a situation that later and in its turn requires further therapy At this later date the original injury has long since healed and although originally arising as a complication of the former, the later condition will be an entity in itself and have its own signs symptoms and pathology and require its own specialized therapy Necessary treatment for this type of complication invariably is surgical

Bilateral Subtemporal Decompression

As the result of necessary operative procedures patients who have sustained cranio cerebral injuries are left at times with bilateral temporal bony defects If both are of any significant size late closure of at least one may prove to be essential to the patient s final and complete recovery

Pathology — There is an absence of a part of the squamous temporal and often adjoining portions of the frontal and parietal bones on both sides of the skull The bone defects overlie defects in the dura which are of approximately the same size The vertical or inverted horseshoe

the scalp the meninges the bone edges and the cortex Previous infection increases this tendency to mat together

Symptoms — Unless the dural opening is large these symptoms usually are limited to a feeling of insecurity and to the irritation and fear caused by the consciousness of a visible deformity

Signs — The objective sign is a visible or palpable depression under the scalp at the site of the absent bone Pulsation may or may not be visible usually not in the older ones but except in the small trephine hole defects usually is palpable

Treatment — The preferable method of closure depends upon the size of the bony opening that is to be filled The material used should if possible always be in the nature of an osteo periosteal transplant This transplant is obtained most easily even for large defects from adjacent areas of skull To obtain it an appropriately sized piece of outer table to which periosteum is still attached is removed in one piece and moved into the defect This procedure is known as the Konig Mueller operation For small defects a button of bone from an area within the hair line may be removed with the old fashioned hand button trephine and used to fill the deficiency that is visible Bone chips and bone fragments may be used also in small defects In all cases however the asepsis must be absolute hemostasis most meticulous and manipulations gentle since sepsis whether from a previously contaminated wound a hematoma or tissue necrosis from improperly handled tissue or too tight sutures will cause the wound to break down and the transplant to be extruded as a foreign body Practically every reasonable material has been recommended and used for the repair of bone defects in the skull Included have been silver plates perforated and non perforated celluloid pieces of ribs and costal cartilages homogenous and heterogenous bone bone obtained at post mortem and subsequently sterilized and bone flaps and fragments of comminuted fractures whether compounded or not No method or material has been as generally satisfactory as the Konig Müeller and the transplant from the adjacent outer table however

Foreign Bodies in Cranio-Cerebral Wounds

This complication manifests itself in such wounds in much the same way that it does in any surgical wound In the absence of infection a foreign body may remain in place for years and cause no symptoms whatsoever If infected however the wound will not heal permanently until the foreign body is removed In cranio cerebral wounds the usual foreign bodies are silk stitches or knots silver clips forgotten pieces of

frontal Deficiences in the *temporal* and *occipital* bones being in the former instance beneath the temporal muscles and in the latter under the heavy neck muscles do not require repair provided the dura is intact

Supra orbital Defects — These are of two types and are classified in accordance with whether the supra orbital ridge is absent or not In neither case is there any involvement of the frontal sinus If the ridge is gone there is little that can be done to correct the defect and replace the ridge Like the frontal sinus fistulas this is a problem which should be referred to and will tax the ingenuity of the plastic surgeon The best cure is prevention The supra orbital ridge usually is absent because it has been removed as part of the treatment of a compound fracture in this region This removal should never be permitted under any circum stances if it is at all po sible to avoid it

Those defects that form part of a fistulous tract which leads into an air sinus usually frontal must be cared for by a surgeon skilled in the more complicated methods of plastic repair and do not properly come within the scope of this discussion

Parieto Frontal Defects — The filling of deficiences of the parietal and frontal bones exclusive of the supra-orbital regions commonly is advised for one of three reasons The first is cosmetic and applies only to those defects that are outside of the patient s hair line The second is because the patient is fearful that the presence of the defect will render him more liable to injury than he would be if the skull was intact This fear is justified only in the larger defects but it should not be overlooked that even if not justified by the size and location of the deficiency the fear itself may get so out of hand as to affect the patient s morale and even tually to produce a neurosis In such cases justification for the reparative procedures may be found in the emotional effect rather than the anatomi cal size of the defect The third reason commonly is thought to lie in the patient s greater liability to convulsive seizures or peripheral palsies while the artificial opening remains unclosed It cannot be emphasized too strongly that the absence of bone in these conditions has absolutely noth ing to do with either the initiation or continuance of convulsive seizures or peripheral palsies These distressing complications arise out of cortical and subcortical pathology that varies all the way from scar tissue and widespread cellular destruction to adhesions between the cortex and scalp Replacement of absent bone will do nothing for such symptoms unless and until it is accompanied by appropriate excision of cortical scars re lease of adhesions and repair of dural defects

Pathology — The pathology of bony defects is that associated with the absence of both tables of bone locally and associated adhesions between

should be done to keep the intra cranial pressure constantly at or below the normal level

Fungus Cerebri

This is an apparent protrusion of the cortex through coinciding openings in the dura bone and scalp and occurs only in cranio cerebral injuries when there is a severe infection in the wound Meningitis encephalitis septicemia and osteomyelitis usually are present as well Its presence is due to a combination of increased intracranial pressure plus a rapid growth of excessive amounts of granulation tissue on the surface of the infected brain From the therapeutic point of view it is important only because it must not be cut off To do so leads only to its regrowth to an even larger size or what is more likely to a spread of the encephalitis and death of the patient It will disappear without further treatment when the infection has been controlled and the intracranial pressure re-established permanently at normal

Incontinence and Lumbar Puncture

It is at times necessary to do many lumbar punctures in a patient who remains incontinent of urine for a relatively long time If uncorrected such constant lying in a wet bed will produce a high incidence of infection in the skin puncture wounds and may lead to meningitis Even at the best it forces the operator to reduce the number of his punctures to a minimum that is unsatisfactory and inefficient from the point of view of the cranio cerebral lesion This can be avoided by the use of the tidal drainage apparatus for the bladder Such an apparatus will keep the patient dry obviate residual urine reduce the severity of the infection that is associated with other types of constant drainage of the genito urinary tract prevent shrinkage or distention of the urinary bladder and simplify what is otherwise a very difficult nursing problem If the apparatus is adjusted properly either male or female patients can wear an inlying urethral catheter indefinitely provided only that it be removed cleaned and sterilized once a week The apparatus must be sterilized also at the same time and care taken to see that the irrigation fluid is kept free of contamination by bacteria at all times

Cranio Cerebral Injury in the New born

Although not commonly recognized as being part of the problem of cranio cerebral injuries it is nevertheless true that intracranial hemorrhage

cotton broken pieces of drainage material unabsorbed muscle postage stamp grafts and dead bone

Broken Lumbar Puncture Needles

The breaking of a lumbar puncture or long injection needle is or should be recognized at the time it occurs and at least at the finish of the puncture by the discovery of the break when the needle is withdrawn It is an occasional unavoidable accident inherent in the treatment of uncooperative and at times maniacal patients The patient will complain of no symptoms and may not know of the incident The fragment usually is in the lumbar but may be in the high cervical region

Pathology — The fragment is never wholly in the spinal canal at first For a variable period of time after the break some part of it will be found sticking through the ligamentous structures or into the bony wall

Symptoms and Signs — Beyond identifying the site of the puncture in the skin physical examination will yield little information X ray examination on the other hand is essential This should be made at once Stereoscopic films in both the lateral and anteroposterior planes should be taken Following the x ray examination the patient should be moved as little as possible to avoid shifting the position of the fragment

Treatment — This should consist of the operative removal of the fragment as soon as possible The operation should be formal and no time should be wasted in trying to find the fragment through a small incision with an inadequate kit and no assistance It should be carried out through a trap door incision which is hinged on one side of the mid line and shaped like a half circle in the centre of which is the approximate location of the needle end In this way a segment of a circle will be turned across the mid line which if cut to a proper depth will expose the lumbar fascia The end of the needle usually is visible at this point but if not a similar trap door of fascia turned in the other direction can be cut Further steps follow those of the classical laminectomy

Post operative Cerebro Spinal Fluid Fistulas

The drainage of cerebro spinal fluid through a fistulous opening in an operative wound that is uninfected and that does not include a foreign body usually can be controlled by the frequent application of large amounts of thymol iodide If this is not effective the wound should be incised the fistulous tract removed and the wound carefully resutured layer by layer with interrupted silk stitches Enough lumbar punctures

should be done to keep the intra-cranial pressure constantly at or below the normal level

Fungus Cerebri

This is an apparent protrusion of the cortex through coinciding openings in the dura bone and scalp and occurs only in cranio cerebral injuries when there is a severe infection in the wound Meningitis encephalitis septicemia and osteomyelitis usually are present as well Its presence is due to a combination of increased intracranial pressure plus a rapid growth of excessive amounts of granulation tissue on the surface of the infected brain From the therapeutic point of view it is important only because it must not be cut off To do so leads only to its regrowth to an even larger size or what is more likely to a spread of the encephalitis and death of the patient It will disappear without further treatment when the infection has been controlled and the intracranial pressure re-established permanently at normal

Incontinence and Lumbar Puncture

It is at times necessary to do many lumbar punctures in a patient who remains incontinent of urine for a relatively long time If uncorrected such constant lying in a wet bed will produce a high incidence of infection in the skin puncture wounds and may lead to meningitis Even at the best it forces the operator to reduce the number of his punctures to a minimum that is unsatisfactory and inefficient from the point of view of the cranio cerebral lesion This can be avoided by the use of the tidal drainage apparatus for the bladder Such an apparatus will keep the patient dry obviate residual urine reduce the severity of the infection that is associated with other types of constant drainage of the genito urinary tract prevent shrinkage or distention of the urinary bladder and simplify what is otherwise a very difficult nursing problem If the apparatus is adjusted properly either male or female patients can wear an inlying urethral catheter indefinitely provided only that it be removed cleaned and sterilized once a week The apparatus must be sterilized also at the same time and care taken to see that the irrigation fluid is kept free of contamination by bacteria at all times

CRANIO CEREBRAL INJURY IN THE NEW BORN

Although not commonly recognized as being part of the problem of cranio-cerebral injuries it is nevertheless true that intracranial hemorrhage

of the new born and the general problem of fetal cranio cerebral injuries produced before and during labor should be included therein To be sure the pathology is conditioned somewhat by the method of production and the antecedent circumstances but from the larger point of view it is now possible just as in the adults to identify a common fundamental non operable group of lesions to which may be added certain operable conditions bony and meningeal injuries and complications arising out of general bodily states and local infection

While fetal cranio cerebral injury unquestionably is associated always with the general problem of labor the primary causative factor is found not in the application of external violence to the head but rather in a pathological extension of a normal physiological process It has now been established beyond reasonable doubt that the full term human fetus normally exists in the uterus in a state of cyanosis With this goes a blood oxygen unsaturation that is nearly twice that sufficient to make the cyanosis visible At birth this oxygen unsaturation is increased by one quarter because of the impairment of the placental circulation by the contracting uterus Thus at this time the arterial blood of the fetus contains less oxygen than the venous blood of the mother Any increase in this oxygen unsaturation will be pathological It will be associated with tissue anoxia and marked generalized venous congestion and is by definition asphyxia It will vary in degree and may produce a wide variety of tissue changes including edema petechial and coalescing hemorrhages thrombosis cellular destruction an accumulation of lactic acid in the blood stream alterations in the respiratory and pulse rates a fall in blood pressure to shock levels and finally death The asphyxia affects the entire fetus and all its organs including the brain It is produced by an interference with the placental circulation and may therefore be present long before labor has begun Since it is probable that the normal fetus in utero makes respiratory movements which are continued as normal breathing coincident with the termination of the placental circulation inhalation of vernix meconium and liquor may take place before or during labor Their mechanical obstructive effect may render the already existent asphyxia more asphyxial It should be emphasized that pathological asphyxia cannot be measured in terms of either cyanosis or absolute anoxemia and its presence can be recognized only by a demonstration of abnormalities in the placental circulation or of signs known to be associated with tissue anoxia of high degree The organs most commonly the seat of resultant demonstrable changes are the liver lungs heart kidneys intestinal tract spleen adrenals thymus spinal cord and brain The seat or seats of such maximum involvement will determine the symptomatol

ogy while trauma locally only increases the extent and severity of this damage to any underlying structure

Fundamental Intracranial Pathology in Cranio Cerebral Injuries of the New Born

Insofar as it affects the brain the basic asphyxia of the new born and its after-effects are completely analogous to the vasovagal reflex and the changes it institutes in the adults Associated with and resulting from the asphyxia may be an increased cerebral venous pressure congestion and dilation of the venules perivascular and perineuronal edema congestion and dilatation of the cerebral veins an increase in intracranial and cerebrospinal fluid pressure cortical and subcortical thromboses and petechial and coalescing hemorrhages and finally rupture of the external and larger veins Such changes if appropriately placed and of sufficient extent as the result of the asphyxia alone may terminate in all degrees of cortical and subcortical cellular destruction In later life these end results may be apparent as disturbances varying from porencephaly and hydrocephalus ex vacuo through epilepsy and idiocy to any degree of spastic paraplegia or Little s disease In the earlier fatal cases autopsy if death has been due to the intracranial condition may demonstrate intraventricular subarachnoid and subpial hemorrhages complicating cerebral cerebellar and medullary edema and limited only by the size and location of the ruptured vein If the intracranial condition is merely a minor complication of other fatal organic injuries then there may be no more than cerebral congestion and edema Thus the diagnostic possibilities as applied to the cranial contents of the newborn vary from congestion and edema through intracortical subarachnoid and subpial hemorrhages to intraventricular hemorrhage from rupture of the vessels of the choroid plexus but the etiology is the same in every case and is found in the fetal asphyxia All these conditions are analogous to the non-operable cerebral lesions in the adult To them are added the changes that result directly from trauma They are classed as a group under the name of *asphyxial type of intracranial injury in the new born*

Additional Cranial and Intracranial Pathology in Cranio Cerebral Injuries of the New Born

The more extensive and additional pathology that is commonly associated with varying degrees of trauma to the fetal head never occurs alone but always as an accompaniment of the results of the associated

fetal asphyxia However, it may prove to be impossible, in a given case to separate causes and results from one another or even to be sure whether trauma actually has been a factor or not Consequently it is only in the clear cut cases that this latter diagnosis can be added to that of asphyxial intracranial damage as an explanation of the symptoms or post mortem findings Attempts to diagnose completely every case should be persisted in however because a demonstration of a traumatic factor in the causation of the symptoms may prove to be the one thing needed to justify the predication of an operable lesion This if treated at once and properly may be prevented from causing death or what is worse prolonged invalidism followed by death

The sources of such trauma are various Some arise commonly but not necessarily out of methods adopted by the obstetrician to terminate labor The less obvious but more usual sources are found in the processes of labor itself however The former predicate an unsatisfactory or difficult labor as the reason for termination and therefore of necessity also predicate a high degree of fetal asphyxia Compression of the head by the application of such external force will at the very least increase the venous congestion and rupture veins that otherwise would not break or lead to a more serious edema with its associated wider spread of anoxia and cellular damage It is characteristic of both kinds of trauma however to be of a type the application of which is relatively slow and prolonged This is in contradistinction to the methods by which adult injuries are caused Whether produced by some such procedure as the misapplication of high forceps or whether due to some type of uterine dystocia the ultimate effect is the same and results in a slow intermittent squeezing of the skull This leads to an excessive overriding of the individual bones Some degree of this moulding is a normal accompaniment of all labor When carried beyond this point however its harmlessness depends upon the margin of extensibility of the bridging veins which cross from the cortex to the venous sinuses the elasticity of the dural septa and the degree of compression of the cranial ends of the jugular veins Thus early rupture of the membranes with a dry labor cephalopelvic disproportion with arrest of the descent of the head or prolongation of the second stage of labor from a stiff undilatable cervix and the like all lead to excessive increase in venous congestion locally The bridging veins become overdistended and their potential powers of elongation thus are done away with This factor together with no more than normal overlapping at the suture lines may cause them to rupture When in addition excessive overlapping is required because of delivery from an unfavorable position a small pelvis the application of forceps with traction

or injudicious traction on the head in a breech delivery it is obvious that not only will the bridging veins rupture but that such strain is put upon the falx and tentorium as to cause them to tear and in turn lead to rupture of the vein of Galen and the laceration of the walls of any of the venous sinuses Further traumatic excesses such as a delivery by the Scanzoni maneuver the forceable traction of the fetal head past a protuberant promontory or through a rachitic flat pelvis or strong traction on badly misapplied forceps only add more trouble in the form of fractures through the foramen magnum with or without a broken neck depressed and egg shell fractures and expanding lesions such as result from a rupture of the middle meningeal artery Any of these major injuries may be accompanied by surgical shock This has been unrecognized as such in the past because it has masqueraded under the fanciful title of asphyxia pallida Regardless of whether or not the traumatic origin can be determined in detail all of this type of pathology has as a foundation the cerebral congestion edema and possible hemorrhage that has had its origin in the fetal asphyxia which preceded or accompanied the trauma

Hemorrhagic Disease of the New Born

While not as yet completely understood it is now apparent that the condition that previously has gone under this name is common to all new born It is undiagnosable and probably is something in the nature of a hemorrhagic diathesis While symptoms are caused by it in a minority of cases it has a high mortality when it does cause trouble and if treatment is not instituted promptly The best practice today therefore is to assume that all new born are subject to this complication and therefore should have especially if not normal an early prophylactic and preventive dose of parental whole blood

History and Symptomatology of Cranio cerebral Injury of the New Born

In general cranio cerebral injury of the new born is associated most frequently with the first pregnancy It has been noted however as a complication of all pregnancies up to and through the fourteenth This relationship however is only one of a number of factors that influence its development A study of the graph reproduced herewith (Fig 1) from an article by Clifford and Irving demonstrates at once that the occurrence of cranio cerebral injury in the new born is dependent upon a wide variety of factors and that its prevention is dependent upon a better understand

fetal asphyxia However, it may prove to be impossible in a given case to separate causes and results from one another or even to be sure whether trauma actually has been a factor or not Consequently it is only in the clear cut cases that this latter diagnosis can be added to that of asphyxial intracranial damage as an explanation of the symptoms or post mortem findings Attempts to diagnose completely every case should be persisted in however because a demonstration of a traumatic factor in the causation of the symptoms may prove to be the one thing needed to justify the predication of an operable lesion This if treated at once and properly may be prevented from causing death or what is worse prolonged invalidism followed by death

The sources of such trauma are various Some arise commonly but not necessarily out of methods adopted by the obstetrician to terminate labor The less obvious but more usual sources are found in the processes of labor itself, however The former predicate an unsatisfactory or difficult labor as the reason for termination and therefore of necessity also predicate a high degree of fetal asphyxia Compression of the head by the application of such external force will at the very least increase the venous congestion and rupture veins that otherwise would not break or lead to a more serious edema with its associated wider spread of anoxia and cellular damage It is characteristic of both kinds of trauma however to be of a type the application of which is relatively slow and prolonged This is in contradistinction to the methods by which adult injuries are caused Whether produced by some such procedure as the misapplication of high forceps or whether due to some type of uterine dystocia the ultimate effect is the same and results in a slow intermittent squeezing of the skull This leads to an excessive overriding of the individual bones Some degree of this moulding is a normal accompaniment of all labor When carried beyond this point however its harmlessness depends upon the margin of extensibility of the bridging veins which cross from the cortex to the venous sinuses the elasticity of the dural septa and the degree of compression of the cranial ends of the jugular veins Thus early rupture of the membranes with a dry labor cephalopelvic disproportion with arrest of the descent of the head or prolongation of the second stage of labor from a stiff undilatable cervix and the like all lead to excessive increase in venous congestion locally The bridging veins become overdistended and their potential powers of elongation thus are done away with This factor together with no more than normal overlapping at the suture lines may cause them to rupture When in addition excessive overlapping is required because of delivery from an unfavorable position a small pelvis the application of forceps with traction

or injudicious traction on the head in a breech delivery it is obvious that not only will the bridging veins rupture but that such strain is put upon the falx and tentorium as to cause them to tear and in turn lead to rupture of the vein of Galen and the laceration of the walls of any of the venous sinuses Further traumatic excesses such as a delivery by the Scanzoni maneuver the forceable traction of the fetal head past a protuberant promontory or through a rachitic flat pelvis or strong traction on badly misapplied forceps only add more trouble in the form of fractures through the foramen magnum with or without a broken neck depressed and egg shell fractures and expanding lesions such as result from a rupture of the middle meningeal artery Any of these major injuries may be accompanied by surgical shock This has been unrecognized as such in the past because it has masqueraded under the fanciful title of asphyxia pallida Regardless of whether or not the traumatic origin can be determined in detail all of this type of pathology has as a foundation the cerebral congestion edema and possible hemorrhage that has had its origin in the fetal asphyxia which preceded or accompanied the trauma

Hemorrhagic Disease of the New Born

While not as yet completely understood it is now apparent that the condition that previously has gone under this name is common to all new born It is undiagnosable and probably is something in the nature of a hemorrhagic diathesis While symptoms are caused by it in a minority of cases it has a high mortality when it does cause trouble and if treatment is not instituted promptly The best practice today therefore is to assume that all new born are subject to this complication and therefore should have especially if not normal an early prophylactic and preventive dose of parental whole blood

History and Symptomatology of Cranio-cerebral Injury of the New Born

In general cranio cerebral injury of the new born is associated most frequently with the first pregnancy It has been noted however as a complication of all pregnancies up to and through the fourteenth This relationship however is only one of a number of factors that influence its development A study of the graph reproduced herewith (Fig 1) from an article by Clifford and Irving demonstrates at once that the occurrence of cranio-cerebral injury in the new born is dependent upon a wide variety of factors and that its prevention is dependent upon a better understand

ing and management of the whole pregnancy from the first months until after the umbilical cord is divided

In addition to the general historical background as noted above, certain specific data will carry additional diagnostic weight For example a story of any significant variation in the fetal heart rate of the excessive administration of inhalation anesthetics to the mother or the use of morphine previous to delivery of a primiparous or a prolonged or dry labor and an anomaly of the umbilical cord all suggest the possibility of an

CRANIO CEREBRAL INJURIES

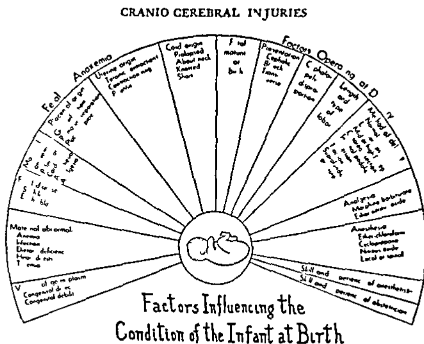


FIG 1 The etiological possibilities in the production of cranio-cerebral injury in the new born Reproduced from Surgery Gynecology and Obstetrics Vol 65 p 24 July 1937 through the courtesy of the Surgical Publishing Company of Chicago Illinois.

asphyxiated baby Prolonged cyanosis meconium in the amniotic fluid difficulty in starting the baby s respiration and possibly general flaccidity and pallor at birth will strengthen such a supposition Should there be in addition a history of a difficult rough labor dystocia of the birth canal bad application of forceps delivery face to pubes or from other unfavorable positions and enough pallor and flaccidity to suggest the possibility of surgical shock then the physician will do well to suspect a traumatic type of intracranial pathology in addition to the changes that he should expect after asphyxia

Signs and Symptoms

These are common to both types of intracranial injury in the new born. They are present at once after birth and in all possible combinations. The commonest are hypertonicity, an abnormal or poor cry, cyanosis and failure to nurse. The hypertonus is best demonstrated by the presence of increased reflexes and more particularly by a characteristic excessive muscular reaction to excessive sensory stimuli. The typical abnormal cry is a sudden shriek, but it may also be absent suggesting unconsciousness, continuous suggesting meningeal irritation, or vary in volume, tone or frequency. Cyanosis is more frequent in the fatal cases. It may or may not be associated with abnormal respiration. Failure to nurse indicates loss of the sucking reflex and will be noticeable both when the baby is put to breast or given the bottle. The fontanelles usually are tense but by no means always. Apathy and abnormality of respiration are common. The latter should not be mistaken for mechanical laryngeal stenosis such as caused by an enlarged thymus gland. Flaccidity, pallor and birth asphyxia frequently appear in combination and usually are associated with apathy, a poor cry, failure to nurse and abnormal respiration. This syndrome has been given the name of asphyxia pallida or pallid asphyxia. The title is descriptive but of no diagnostic value. It should be changed to surgical shock since these symptoms occur in association with a subnormal intracranial pressure, extensive cranial and intracranial damage and in animals, a low blood and pulse pressure.

The intracranial pressure in the absence of surgical shock or dehydration is increased. In the new born it is more convenient to measure the cerebrospinal fluid with a mercury manometer because this type calls for no associated loss of fluid into the manometer. Normal pressure varies between 2 and 5 millimeters of mercury which is equivalent to 30 to 75 mm of water. Variations may extend from a high of 50 mm of mercury (750 mm water) to a low of less than 1 mm of mercury (13 mm of water). Puncture of the cisterna magna is unnecessary, dangerous and should not be practised.

Treatment

In general treatment is governed by the pathology as expressed in the diagnosis and differs in no essential from that given adults in analogous situations. Specifically there are three fundamental procedures. (1) No active therapy other than occasional blood transfusions is permissible while the patient is in surgical shock. Absolute quiet and rest with ex

ternal heat and small amounts of fluid by mouth through a medicine dropper usually are sufficient Blood transfusion if done skillfully and without creating a disturbance or requiring movement of the baby from its crib may be done but only under such conditions In the severe cases it may prove helpful to give one drachm (4 c c) of saturated solution of magnesium sulphate by rectum to be retained (2) When the infant s out of surgical shock a prophylactic transfusion of 30 to 60 c c of parental whole blood should be given No typing or grouping is required during the first 10 days of life The blood may be given into any convenient vein except the superior sagittal sinus (3) The increased intracranial pressure must be treated now This is done best by repeated lumbar punctures with removal of enough cerebrospinal fluid at each one to reduce a high pressure to normal figures Manometric pressure measurements must be made Punctures should be repeated at least every 24 hours until two successive normal pressures have been read previous to the withdrawal of any cerebrospinal fluid The puncture requires no anesthesia is best made with an adult sized needle and in any interspace between the 12th thoracic and the 5th lumbar Exploratory trephination or the less satisfactory procedure of needle puncture of the anterior fontanelle may be resorted to provided the patient fails to improve under this non-operative treatment and provided the physician wishes to rule out certainly the complicating presence of an expanding lesion such as a sub or extra dural hematoma Elective operations such as that required for the elevation of a depressed fracture invariably should be postponed until the intracranial pressure has been reestablished at normal

In addition to the above specific therapeutic requirements it will be well to abide by certain general rules also These affect the baby s general condition and have as their object the maintenance of as nearly complete rest as possible together with the administration of a sufficient quantity of fluid and food In the furtherance of this aim the baby should not be moved from the crib for any purpose whatever and should be handled in the crib as little as possible Food and fluid should be given by a Breck feeder or gavage until the patient can take the bottle without danger of tiring Fluids should be given by mouth if possible at the rate of 2 to 3 ounces per pound of weight per 24 hours If mouth feeding is impossible or inadequate salt solution should be given by clysis If the rate of administration is adjusted properly and the clysis continuous several hundred c c of fluid may be given thus into the rectum during 24 hours Oxygen may be given for cyanosis Convulsions are treated best by lumbar punctures Magnesium sulphate intramuscularly may be given in addition Morphine in any form is contra indicated The effect of the

relationship of the height of the feet to that of the head varies and is best determined by experiment

The Non Operable Intracranial Injuries of the New Born

The vast majority of the intracranial injuries of the new born fall into this class There are two reasons for this first because the pathology associated with asphyxia is omnipresent and as such does not require operative therapy and second because the extent and severity of the results of trauma are such that additional local trauma even though under the guise of a craniotomy predicates immediate death for the patient

Asphyxial Intracranial Injury of the New Born

The commonest intracranial lesion of the new born is one that is due to the changes associated with asphyxia

Pathology — In the early stages the pathology will vary all the way from cerebral congestion and edema through subcortical thromboses petechial and coalescing hemorrhages and varying amounts of cellular and subcortical destruction to hemorrhages in the perineuronal perivascular subpial and subarachnoid spaces and into the cavities of the ventricles If the patient survives and has been treated poorly or not at all and in a certain percentage even if the best of therapy has been provided permanent changes result These vary from porencephalic cysts general or local cortical or subcortical atrophy or scars and cortico meningeal adhesions to hydrocephalus ex vacuo

Symptoms and Signs — These have been covered adequately in the preceding sections

Diagnosis — The diagnosis is made from the history and the lumbar puncture findings

Treatment — This is directed toward relieving the increased intracranial pressure It is done by dehydration or lumbar decompression or both The dehydration should be carried out in these new born with considerable care as there is a much smaller margin of safety between the therapeutic and the toxic varieties than there is in the adults or older children It is best accomplished by the use of magnesium sulphate by rectum or intramuscularly The dose by rectum is not over 1 drachm (4 c c) of the saturated solution It should not be repeated more than once and then only after 4 hours If used intramuscularly 7½ minims (½ c c) of a sterile 50 per cent solution is given every 3 or 4 hours If the injection is made deeply into the muscle there is little danger of

causing a slough Lumbar decompression is the preferable method This has been sufficiently described previously Operation as a method of treatment is contra indicated It may be used however as an exploratory diagnostic procedure to rule out a suspected sub or extra dural hematoma after a period of non operable therapy has failed to afford relief It should be preceded usually by a trans fontanelle subdural puncture for the same purpose (See also *Ratio of Occurrence and Mortality of Intra cranial Hemorrhage of New Born* on a subsequent page)

The Inoperable Traumatic Cranial and Intracranial Injury in the New Born

The patients that fall into this group have the results of trauma super imposed upon a background of pathology that is primarily due to changes produced by asphyxia

Meningeal Tears Ruptures of Venous Sinuses the Vein of Galen and the Internal Cerebral Veins

Pathology — Meningeal tears result from such a degree of moulding of the fetal head as will put an excessive strain on the tentorium or falx or both The direction of the greatest deformity will determine which partition sustains the greatest damage The extent of the deformity determines the amount of damage and the liability of involvement of the venous sinuses and the vein of Galen system The simplest injury is represented by the harmless and avascular tears of the body of the falx or the splitting of the superior layer of the tentorium at its junction with the falx More extensive injuries extend the tears into the superior sagittal the lateral and the straight sinuses Occurring either alone or in conjunction with any of the above the vein of Galen or either or both of its tributaries the internal cerebral veins may be ruptured These latter and more extensive injuries necessarily are associated with wide spread and massive meningeal and ventricular hemorrhages These may cover the entire surface of the cerebrum cerebellum and brain stem and completely fill the entire ventricular system

Symptoms and Signs — These have been adequately covered in the preceding sections

Diagnosis — The detailed diagnosis can be made only at autopsy It may be inferred from the history and the findings at lumbar puncture

Treatment — The only possible and effective treatment is that which will care for the associated asphyxial intracranial pathology and the in

creased intracranial pressure This has been covered above Operations of any type are contra indicated (See also *Ratio of Occurrence and Mortality of Intracranial Hemorrhage of New Born* on a subsequent page)

Non Complicating Fractures of the Skull in the New Born

These fractures may involve any of the cranial bones and as in the adult are of themselves harmless They serve only as a measure of the type and amount of force that has been applied to the cranium There is however a fairly constant relationship between the etiology and the location of the break Misapplication of forceps will produce eggshell fractures at the point or points that correspond to the tips of the blades Traction of the head through forceps however applied plus a combination of bending and twisting the neck as in the Scanzoni maneuver will cause a fracture of the base of the skull that usually includes the foramen magnum and is complicated by a broken neck

Pathology — The pathology in addition to that produced by the associated asphyxia is adequately described in the one instance as an egg shell fracture of a flat bone and in the other as a comminuted or linear fracture in or near the foramen magnum

Signs and Symptoms — These have been described adequately above

Diagnosis — The diagnosis is made on the history and lumbar puncture findings and at autopsy

Treatment — The only effective and possible treatment is that directed toward correcting the results of the associated pathology that has followed the accompanying asphyxia This has been discussed sufficiently above It is in these cases that prophylaxis proves to be the best therapy (See also *Ratio of Occurrence and Mortality of Intracranial Hemorrhage of New Born* on a subsequent page)

The Operable Cranial and Intracranial Injuries of the New Born

The operable cranial and intracranial injuries in the new born are made up of the expanding meningeal hemorrhages and the depressed fractures Both are present in addition to the pathology that is produced because of asphyxia

Subdural Hematoma

Pathology — Subdural hematomas in the new born as far as is known at present are due to the rupture of a bridging vein where it crosses the

causing a slough Lumbar decompression is the preferable method This has been sufficiently described previously Operation as a method of treatment is contra indicated It may be used however as an exploratory diagnostic procedure to rule out a suspected sub or extra dural hematoma after a period of non operable therapy has failed to afford relief It should be preceded usually by a trans fontanelle subdural puncture for the same purpose (See also *Ratio of Occurrence and Mortality of Intra cranial Hemorrhage of New Born* on a subsequent page)

The Inoperable Traumatic Cranial and Intracranial Injury in the New Born

The patients that fall into this group have the results of trauma super imposed upon a background of pathology that is primarily due to changes produced by asphyxia

Meningeal Tears Ruptures of Venous Sinuses the Vein of Galen and the Internal Cerebral Veins

Pathology —Meningeal tears result from such a degree of moulding of the fetal head as will put an excessive strain on the tentorium or falx or both The direction of the greatest deformity will determine which partition sustains the greatest damage The extent of the deformity determines the amount of damage and the liability of involvement of the venous sinuses and the vein of Galen system The simplest injury is represented by the harmless and avascular tears of the body of the falx or the splitting of the superior layer of the tentorium at its junction with the falx More extensive injuries extend the tears into the superior sagittal the lateral and the straight sinuses Occurring either alone or in conjunction with any of the above the vein of Galen or either or both of its tributaries the internal cerebral veins may be ruptured These latter and more extensive injuries necessarily are associated with wide spread and massive meningeal and ventricular hemorrhages These may cover the entire surface of the cerebrum cerebellum and brain stem and completely fill the entire ventricular system

Symptoms and Signs —These have been adequately covered in the preceding sections

Diagnosis —The detailed diagnosis can be made only at autopsy It may be inferred from the history and the findings at lumbar puncture

Treatment —The only possible and effective treatment is that which will care for the associated asphyxial intracranial pathology and the in

Extradural Hematoma

This is an uncommon lesion in the new born except as one of a number of severe associated cranial injuries Probably it has never been diagnosed during life except by accident

Pathology — The source of the clot usually is found in multiple ruptures of the terminal twigs of the middle meningeal artery These vessels tear at points where they perforate the inner table of the skull to act as nutrient vessels for the bones or to continue through the diploe and outer table to anastomose with one of the scalp arteries They are associated with eggshell fractures of the temporal parietal or frontal bones Other sources are a rupture of one of the cranial venous sinuses in association with other and more extensive injuries or a surgical curiosity a rupture of the trunk or one of the main branches of one of the middle meningeal arteries Since in the new born the dura is continuous through the suture lines with the periosteum the size of the extradural clot necessarily is limited by the size of the bone that it underlies and the elasticity of the dura Its effect on the brain is localized correspondingly

Signs and Symptoms — These are not clear Whatever specific peculiarities exist as the result of this condition are in addition to those due to the associated brain lesion These latter have been discussed sufficiently in previous sections There is no tri partite pathognomonic history as in the adult Convulsions a persistent or increasing hemiplegia a high irreduceable intracranial pressure and tense fontanelles ought to be associated frequently with this condition

Diagnosis — This can be made only by exploratory trephination

Treatment — This is surgical It should include evacuation of the clot closure of the bleeding artery or arteries by ligation or some similar method and a subtemporal decompression The *Ratio of Occurrence* and the *Mortality* are unknown

Depressed Fracture of the Skull

Pathology — This lesion usually is caused by pressure of the baby s head against the promontory of the sacrum or the symphysis pubis It may be caused also by the misapplication of forceps Any bone may be involved The lesion is a characteristic celluloid ball depression without a fracture Mild degrees of asphyxial intracranial damage usually are associated with it

Symptoms and Signs — These are for the most part covered above The special sign that goes with this fracture is a spoon shaped depression

subdural space on its way from the cortex to a major venous sinus or its adjacent dura They may be associated with either the asphyxial or the traumatic type of etiology The veins which are almost always cerebral rupture because they are congested and distended their extensibility is gone and hence when moulding and over riding at an adjacent suture line takes place they are unable to compensate for it by elongation and so break The bleeding end empties into the subdural space and produces a solid subdural hematoma Because there is no associated tear in the arachnoid and hence no admixture of cerebrospinal fluid these hematomas are made up exclusively of blood Their content is therefore, at first fluid then clot with a fluid centre and surrounded by organizing membranes and finally yellow fluid with a high protein content contained within a thick walled fibrous cyst or as represented by a complete fibrous organization They are expansile only during their formation They may therefore be present for periods of months or years without causing any demonstrable alteration in intracranial pressure room being provided within the cranium by a local atrophy of the underlying cortex

Symptoms and Signs —The symptoms and signs are those of the associated asphyxial pathology and have been adequately discussed previously In addition there is some reason to suppose that as a result of the presence of the clot there is in all probability a greater liability on the part of the patient to have a hemiplegia and/or to develop convulsive attacks

Diagnosis —The diagnosis can be made only by exploratory trephination or subdural puncture through the anterior fontanelle One or if necessary both of these procedures should be employed always whenever the infant fails to improve under properly applied non-operative therapy which has been up to that point based on a diagnosis of either asphyxial or traumatic cerebral edema or subarachnoid hemorrhage They should not be delayed unduly

Treatment —Treatment is operative If there are good and sufficient reasons for it an attempt may be made to evacuate the hematoma by repeated subdural punctures through the anterior fontanelle There is today however a considerable accumulation of experience which makes it probable that no better than partial evacuation at the best can be expected from this method Trans temporal trephination if necessary bilateral with evacuation of the hematoma under the direct view of the operator is the procedure of choice for these cases (See also *Ratio of Occurrence and Mortality of Intracranial Hemorrhage of New Born* on a subsequent page)

Extradural Hematoma

This is an uncommon lesion in the new born except as one of a number of severe associated cranial injuries Probably it has never been diagnosed during life except by accident

Pathology — The source of the clot usually is found in multiple ruptures of the terminal twigs of the middle meningeal artery These vessels tear at points where they perforate the inner table of the skull to act as nutrient vessels *for the bones or to continue through the diploe and outer* table to anastomose with one of the scalp arteries They are associated with eggshell fractures of the temporal parietal or frontal bones Other sources are a rupture of one of the cranial venous sinuses in association with other and more extensive injuries or a surgical curiosity a rupture of the trunk or one of the main branches of one of the middle meningeal arteries Since in the new born the dura is continuous through the suture lines with the periosteum the size of the extradural clot necessarily is limited by the size of the bone that it underlies and the elasticity of the dura Its effect on the brain is localized correspondingly

Signs and Symptoms — These are not clear Whatever specific peculiarities exist as the result of this condition are in addition to those due to the associated brain lesion These latter have been discussed sufficiently in previous sections There is no tri partite pathognomonic history as in *the adult* *Convulsions a persistent or increasing hemiplegia a high ir* reduceable intracranial pressure and tense fontanelles ought to be associated frequently with this condition

Diagnosis — This can be made only by exploratory trephination

Treatment — This is surgical It should include evacuation of the clot closure of the bleeding artery or arteries by ligation or some similar method and a subtemporal decompression The *Ratio of Occurrence* and the *Mortality* are unknown

Depressed Fracture of the Skull

Pathology — This lesion usually is caused by pressure of the baby s head against the promontory of the sacrum or the symphysis pubis It may be caused also by the misapplication of forceps Any bone may be involved The lesion is a characteristic celluloid ball depression without a fracture Mild degrees of asphyxial intracranial damage usually are associated with it

Symptoms and Signs — These are for the most part covered above The special sign that goes with this fracture is a spoon shaped depression

in the injured bone It is both visible and palpable and has little or no hematoma around it

Diagnosis — The diagnosis is made from the visible and palpable findings on the skull X rays are of little help

Treatment — This is exclusively operative in as much as these depressions do not elevate themselves The procedure should be formal and one that will permit of an elevation under direct vision in order to avoid causing cortical or meningeal damage Elevation by means of a sharp hook which is used first to perforate the scalp and bone and then to jerk the depression into place is inexcusable After proper elevation the depression will not fall back The operation should never be undertaken except as a procedure of choice and only then after repeated lumbar punctures have made it certain that the associated asphyxial cerebral pathology is righted and the intracranial pressure again established permanently at normal Of itself and provided it is properly treated this lesion should carry no mortality Any bony defect will fill in Under other circumstances the statements made under *Ratio of Occurrence and Mortality of Intracranial Hemorrhage of New Born* on a subsequent page will apply

Complications of Cranial and Intracranial Injuries of New Born

Predictable complications of cranial and intracranial injuries of the new born while not as common as in the similar adult injuries do occur sufficiently often to merit discussion Their mathematical incidence is not known They include surgical shock toxic dehydration intra uterine and post partum infection of the central nervous system and injuries to the soft tissues of the face and scalp

Surgical Shock

This can be made only as a presumptive diagnosis at present Proof of its presence in any given case will be lacking because of the impracticability of measuring blood pressures on these infants However even in the absence of this final proof the presumptive evidence is so strong and its diagnostic importance so great that its presence from the practical point of view should be assumed

Diagnosis — If a baby that is known to have been seriously battered and injured about the head during the course of labor or delivery is pale flaccid unconscious and cyanotic at birth if its temperature is subnormal its intracranial pressure the same and if it bears ample external evidence

of having been severely traumatized the diagnosis of surgical shock should be made A presumptive diagnosis of the same condition should be made also on the objective findings listed above and even in the absence of a traumatic history or in the presence of an asphyxial one

Treatment — The prime requisite of treatment is absolute rest and quiet with sufficient fluids internally and heat externally Blood transfusion if it can be done without moving the baby at all will be helpful (See also *Ratio of Occurrence and Mortality of Intracranial Hemorrhage of New Born* on a subsequent page)

Toxic Dehydration

This condition in the new born is exactly like that in the adult It arises from the same causes overheating including fever insufficient fluid intake diarrhea and vomiting it mimics or reproduces the symptoms of increased intracranial pressure it is characterized by sunken fontanelles low intracranial pressure dry shrunken skin that has lost its elasticity and fever the hematocrit reading of the blood may be extremely high and it is cured by the administration of sufficient fluids to produce hydration Hydration usually will require an intake of from 30 to 60 c c of total fluid per ½ kilo (2 34 pounds) of body weight during each 24 hour period It can be given by mouth or by constant drip clysis

Ratio of Occurrence — This is not known but probably is high

Mortality — If the condition is unrecognized and therefore not treated this is high

Central Nervous System Infection

An infection that is directly attributable to the cranio cerebral injury itself is rare but by no means unknown It is in the form of the classical purulent meningitis *Treatment* is ineffective although sulphanilamide may be tried *Mortality* is 100 per cent

Fetal Meningitis has occurred once in my experience The disease ran its full course before delivery and the diagnosis was made only by the microscopic appearance of the brain and meninges

Contusions of the Face and Scalp Cephalhematomas and Caput Succedaneum

Contusions of the face and scalp may be produced either in the natural course of labor or by the misapplication of forceps They may include

the eye and ear They are of little consequence unless one of the facial nerves has been damaged Under such circumstances particular care should be given the eye Complete interruption of the nerve in front of the ear can occur but is rare It has been recommended that if such a condition is present, and there is in addition a complicating overlying tear of the skin of the face the facial nerve should be explored at once and sutured if need be

Cephalhematomas are subperiosteal hemorrhages As such after two weeks enough bone may be laid down in the lateral wall to give a sensation of crackling when the hematoma is palpated Such bone formation never proceeds beyond this point however The bleeding is limited by the periosteo dural attachments through the suture lines and by the underlying bone Though the hematoma may spread laterally over more than one bone it will not enter the cranial cavity and can have no effect upon the cranial content Rarely in the very large ones enough blood may be lost into it to cause an anemia for which transfusion will be indicated

Treatment —The important thing about treatment is except in the rare emergency of an enormous clot to leave them completely alone In particular they should not be needled incised or drained They will take care of themselves eventually by absorption Invasion of the clot leads to infection in almost every instance This is more important in the new born than in the adult because due to the vascular connections in the former sepsis of the scalp is particularly apt to cause osteomyelitis of the skull

Caput Succedaneum —This is an instance of localized subgaleal edema As such it requires no treatment and in particular should not be needled incised or drained because of the unnecessary and great risk of infection

Ratio of Occurrence and Mortality of Intracranial Hemorrhage of New Born

Those figures that are available give the ratio of occurrence of intra cranial hemorrhage in the new born as varying from 44 per cent in post mortem series to from 2 to 6 per cent as obtained from clinical studies

The immediate mortality can only be approximated It is probably somewhere in the neighborhood of 50 per cent The development of late symptoms that are primarily due to changes originally caused by the birth injury necessarily depends upon the accuracy of the original diagnosis and the efficiency of the treatment in any given case In one series

of cases followed for 7 years hydrocephalus associated with epilepsy or idiocy was the commonest of the unfavorable end results although convulsions alone and spasticity associated with idiocy also occurred Fifteen per cent of this group had such late symptoms Other smaller series that were studied independently yielded the same figure It is probable however that this figure is much too low for the population at large since it is unlikely that the average new born baby is studied and treated as carefully as those in these special series were

First Aid in Cranio Cerebral Injuries

Successful first aid or emergency care of patients with cranio cerebral injuries requires from the doctor the answer to three questions If these are answered correctly and intelligently the ultimate mortality and morbidity will be reduced and later necessary surgical procedures will be simplified with all the benefit to the patient that that implies These questions are (1) Is the patient in surgical shock? (2) Is the injury one that will require treatment by operation within the next 48 hours and if so is the hospital in which he is being examined adequately equipped to handle such a procedure? (3) What is the intracranial pressure and how much blood does the cerebrospinal fluid contain?

Is the patient in surgical shock? — To determine this it is only necessary to measure his systolic and diastolic blood pressures However before proceeding to that it is well for the physician to consider the suitability of the patient s surroundings If for example he is first seen lying out in the road a decision must be reached as to whether or not he should be moved under cover first This decision should be affirmative providing the transportation is limited solely to that requisite to get him under cover Only in this way can unjustified exposure to cold with its increase in shock or to heat with its excessive dehydration be avoided Such movement in addition to being minimal should be made with due regard to any other injuries and in a horizontal position With sufficient help the patient can be moved safely by using his overcoat which is adequate support providing an assistant is assigned to handle the head only This will eliminate the double moving required whenever a stretcher is used It makes no particular difference what kind of a shelter is used provided that it is warm or cool as the weather requires If however a proper ambulance is available and there is room for the patient to lie flat in it there is little added risk in a 20 minute or half hour drive to the nearest hospital This holds particularly true if that institution is adequately equipped to care for this type of emergency

With the patient indoors it is the physician's first responsibility to see to it that his clothes are not removed Such manipulation in the presence of surgical shock may prove all that is necessary to precipitate a fatality Furthermore from a diagnostic point of view such a procedure is of no conceivable use The objection will be raised that with the clothes still in place the presence of coat or dress sleeves will interfere with the use of a sphygmomanometer and the presence of a trouser leg with the treatment of associated injuries of the lower extremities These objections are met adequately and best by slitting the sleeve along the seams and by the application of splints and bandages either over the trouser leg and shoes or directly to the skin after the former has been slit up the seams also Adequate chest and abdominal examinations if they cannot be postponed until after blood pressure readings are available can be made through the loosened clothes their complete removal being superfluous at this time

In any event systolic and diastolic blood pressures should now be measured If the difference between the systolic and diastolic readings the pulse pressure is 15 mm of mercury or lower it may be taken for granted that the patient is in shock If it is 20 mm of mercury or above a second observation must be made at the end of 30 minutes if at the end of that period the systolic pressure has fallen or the pulse pressure decreased the diagnosis of surgical shock again is obligatory Should either or both of these pressures show an increase surgical shock may be considered as being absent If there is no change a third and check reading should be made at the end of another 30 minutes

If thus it has been determined that the patient is in surgical shock then all further examinations any projected transportation and all therapy except for the splinting of broken bones and the treatment of the shock must be abandoned for the time being Since in the usual case of cranio cerebral injury an adequate supply of properly cross matched compatible blood practically is never available any hope for the ideal treatment by blood transfusion must be given up As a substitute however 50 per cent glucose solution may be given intravenously This is stocked by almost every drug store in 50 c c sterile ampoules The adult dose is one or two such ampoules given undiluted Care must be taken to see that the solution does not get into the perivenous tissues as its presence outside of the lumen of a vein is liable to cause local sloughing The dose may be repeated in 2 hours if necessary Salt solution should never be given in the treatment of surgical shock Other therapy includes seeing to it that the patient is kept warm but not overheated has all broken bones properly splinted does not receive morphine or any of its deriva

tives has fluids by mouth in small amounts if conscious empties his bladder if necessary and able to do so and above all is kept completely quiet and not exposed to bright light insurance adjusters anxious relatives and police His head should be kept lower than or on a level with his pelvis unless a complicating chest injury necessitates elevation In this way the physician obtains his answer to the first question of Is the patient in surgical shock? and deals with it appropriately

Is the injury one that will require treatment by operation within the next 48 hours? — The reply to this first part of the second question that the physician must answer will be in the affirmative as far as the cranio cerebral injury goes only if one of three diagnoses can be made or cannot be ruled out The first and most important of these diagnoses is that of an *extradural hemorrhage* The mere suspicion or the probable demonstration of the presence of such a lesion makes it imperative to have the patient in an institution equipped to deal with this major emergency This requirement well may imply transportation for some distance Such a diagnosis at least as a possibility must be made as soon as can be in order that the movement of the patient will have been completed before he is too sick to permit of any help by operation At the time of the injury the diagnosis is made best from the history It should be obtained as accurately as possible and in full detail from the witnesses In particular if the patient is conscious when first seen the greatest care must be taken to determine the presence or absence of any antecedent period of unconsciousness

If the patient can be suspected justly of harboring an extradural clot he must be moved at the earliest possible moment to a hospital equipped with satisfactory staff operating room personnel instruments mechanical aids and available grouped blood donors Within limits the distance to be covered is of no importance in the face of avoiding the tragic necessity of having to do a major operation of this type in an inadequately equipped operating room with untrained or poorly trained staff and no donors After arrival at the selected institution any further procedures necessary to confirm the diagnosis and the necessity for operation can be carried out there These may well include a neurological examination a lumbar puncture with measurements of the cerebrospinal fluid pressure a single x ray plate and so forth

If on the other hand the physician decides that his patient is not suffering from an extradural hemorrhage he must then proceed to ascertain the presence or absence of the second condition that requires operative therapy within the next 48 hours This lesion is a *compound fracture* of the skull Any patient with a scalp wound has a potential fracture of

the skull The first examination then will be to determine whether or not a scalp wound is present If there is no scalp wound there can be no compound fracture of the skull unless it be through the posterior wall of a frontal sinus a condition that does not constitute an emergency If there is a scalp wound the additional presence of a fracture beneath it which is compounded by its presence is best determined by palpation through the wound with one s sterile finger Compounding will be present only if the soft tissues including the periosteum are torn over the fracture line Instruments and other means for examining the wound should not be substituted for the examiner s finger except in the rarest instance The scalp should not be cleansed the hair should be left uncut and in particular the wound must not be irrigated or flooded previous to the palpation If it can be demonstrated that there is a fracture line and that it is compounded nothing literally nothing further should be done at this time except to cover the wound with a sterile piece of gauze and a bandage neither of which should be removed until the patient is anesthetized and on the operating table being prepared for a débridement Compound fractures of the skull require for their proper treatment the same type and amount of equipment and personnel that an extradural clot does That patient therefore that has such a fracture is safer if he is moved than if he is subjected to surgery in a hospital that cannot meet such standards He does not have to be moved however as soon as would be required for the treatment of an extradural hemorrhage Compound fractures need not be debrided within the first 24 hours after their receipt, providing the wound is not manipulated in any way Prophylactic administration of sulphanilamide may be started and continued until the necessity for its use has been confirmed by wound cultures On the other hand debridement must be completed within 48 hours after the receipt of the injury if the surgeon is to keep the patient s chance of morbidity from sepsis down to the proper level of 5 per cent The transportation of the patient with a compound fracture of the skull should be carried out after he is out of surgical shock but soon enough after so that he can have some time to rest at the new hospital before being operated upon and before the 48 hour period has expired

In the absence of both an extradural hemorrhage and a compound fracture of the skull the only other condition that requires operation within 48 hours after receipt of the accident is the condition that is manifested by the *escape of cerebrospinal fluid from the nose* Cerebrospinal rhinorrhea is caused by a fracture into the nose through the cribriform plate one of the ethmoid cells or one of the frontal sinuses Thus it is a compound fracture with the compounding into the nasal cavity rather

than through the scalp The flow of cerebrospinal fluid occurs because a funnel of dura and contained arachnoid has been caught and held in the fracture line The smaller end of this funnel lies in the nose and thus directly connects this cavity with the meningeal spaces It further permits a stream of cerebrospinal fluid to flow constantly from the latter into the former The diagnosis is made by the demonstration of cerebrospinal fluid either alone or at this time more usually mixed with blood dripping from the nostril or into the posterior nasopharynx The latter flow will be recognizable and will come from the nostril when the patient s head is raised The necessity for transportation the need for surgery and the indication for the administration of sulphanilamide in this condition are the same in every detail as that described above for compound fracture of the skull Only one variation exists That lies in the infinitely greater technical difficulty attendant on this operation as compared to that of the ordinary compound fracture of the skull

Thus by virtue of an adequate history the proper examination of the scalp and scalp wounds and observation of the type and amount of nasal discharge in a patient who has just received a cranio cerebral injury one can determine the answer to the second question This will enable the physician to decide whether or not this particular case should be operated upon within the next 48 hours A further decision as to the need for transportation will depend upon the facilities available at the institution where the patient is seen first

What is the intracranial pressure and how much blood does the cerebro spinal fluid contain? This third question can now properly be considered As the answer to this question obviously is to be made by way of a lumbar puncture it will be necessary to undress the patient at least partially Since this is so and since there is no more fuss about completely undressing a person than there is about partially doing so and since if that is done he should be in bed and preferably in a bed where he is to remain permanently it is well to postpone the answer to this third question until it has been settled where he is to be cared for This should never in these cases be at home If the choice involves transportation for any distance up to 250 miles and provided the ambulance is modern and the roads good or adequate train accommodation available he can be moved with perfect safety at this time as far as his cranio cerebral injury is concerned Local conditions will govern the physician s decision to do a lumbar puncture before the transfer As a method of temporizing hypertonic glucose always can be given intravenously at this time and the lumbar puncture done later on Wherever the patient is finally hospitalized however it is now that his clothes are removed for the first time Coin

cidently with this physical and neurological examinations should be done Steps can be taken to treat temporarily any associated injuries An estimation of the amount of cerebral injury can be made and a decision reached about the possibility of permanent therapy for the former and their mutual effects upon each other evaluated A more complete history can be obtained also especially as regards the possibility of dehydration Lumbar punctures must give data in regard to the cerebrospinal fluid pressure the amount of fluid that had to be removed to reduce a high pressure to normal, the amount of macroscopic blood contained in it and the degree of relaxation of the patient Taken in conjunction with his knowledge about the presence or absence of surgical shock and the possibility of dehydration the physician now should be able to determine from this data what type of fundamental cerebral pathology is present Having made this distinction and set it down as concussion edema and congestion or contusion and/or laceration of the brain and having ruled out compound fracture and an extradural hemorrhage the emergency as far as therapy goes is ended Furthermore he has built himself a firm diagnostic foundation upon which he can later if the welfare of his patient requires it erect a superstructure of x ray examinations repeated lumbar punctures exploratory trephinations and other procedures necessary to complete in every detail the diagnostic picture of the patient s injury

Convalescent Care of Cranio Cerebral Injuries

Regardless of the type of injury or the details of the cerebral or bony damage all patients that have sustained a cranio cerebral injury should have their convalescence supervised by a physician He is the only one that is sufficiently detached from the emotional and legal points of view to protect the patient from the psychological assaults of lugubrious friends and relatives and the effects of over developed self interest as fostered by lawyers insurance adjusters and the like

It has been the custom to tell these patients to go home and rest up for periods ranging from a few weeks to many months after their discharge from the hospital Usually the advice is purely empirical and its effects are correspondingly variable and unsatisfactory Analytical study of any cranio cerebral injury will demonstrate that in essence the acute phase differs in no way from that associated with the healing of any wound It is not commonly considered in that light because the wound usually is invisible its progress toward recovery cannot be watched and the diagnosis usually does not serve as a word guide to the pathology The various procedures described in the foregoing sections have to do with the

means for treating the tissues of the skull and brain in such a way that this wound healing can take place under the optimum conditions Hemorrhage is controlled expanding or space occupying clots are removed the intracranial circulation is restored to normal and infection is combated or prevented These requisites having been fulfilled normal healing will progress and cicatrization take place in accordance with the same laws that govern tissue repair in other and more visible parts of the body What variation there is will be found in the inability of the nervous tissue to reproduce destroyed cells and in the difficulty with which the flat cranial bones fill defects that have been created in them Insofar then as these peculiar deficiencies cause destruction and regardless of the wound healing there will result permanent functional loss that is irreparable Such local peculiarities however do not alter the underlying situation Since repair of wounds depends upon the integrity of the blood supply and the efficiency of the oxygenation of the damaged tissues the final stages of wound healing that lead to permanent cicatrization begin when the circulation has returned to normal provided only that infection does not complicate the picture Because of their interdependence this phase starts in cerebral wounds with the return to normal of the intracranial pressure and its stabilization at that level It is at this point that the patient s convalescent period begins and it is from these facts that the starting date is determined

The First Period of the Convalescence

This period is devoted to making certain that the various craniocerebral wounds heal as completely and rapidly as possible To facilitate that and because it lessens the extraneous demands on the patient s metabolism and circulation the patient is kept flat in bed during it If infection is not present any wound should be healed solidly in 10 days especially if the patient is allowed no activity To be on the safe side however this time is extended for 4 more days and the patient kept flat in bed for 2 weeks from the date his intracranial pressure has returned to and become stabilized at normal At the end of that time he is allowed to get out of bed and to start the second phase of his convalescence Appropriate adjustments are made for infected wounds

The Second Period of the Convalescence

This second period is devoted to getting the patient into such good general condition that he can leave the hospital for his home without the

necessity of being invalided at the latter place Because of the traditional mystery associated in the mind of the ordinary layman with brain injuries and the fear of insanity that besets the victim of such accidents these patients will be particularly apt to use the doctor s directions instead of their own initiative when they are faced with a situation that requires the assumption of responsibility They are thus provided with a perfect alibi for the development of any later symptoms These alibis will metamorphose shortly into mechanisms whereby the patient is able to avoid the performances of unpleasant tasks such as earning a living or will serve to rationalize symptomatology that has only a psychotic background The development of a neurosis is particularly apt to occur later therefore unless properly forestalled at this early period This forestalling process is started most easily and most efficiently when the time comes to get the patient out of bed Its essential underlying principle is that the patient shall be kept continually in a position where he is asking to be more active than the doctor is apparently willing to allow As a result he will in spite of himself assume the responsibility for all his actions and therefore the symptoms that may arise out of them In this way any invalidism that he develops will be of his own creation and thus cannot be used as a means of avoiding his inevitable physical recovery

The first step is taken when the physician not the nurse or the interne tells the patient that he can now get out of bed When he asks for how long a period he should be told to stay up until he is tired after which he is to get back into bed again rest and then get up again. Great care is taken to see to it that no time limit is set and that his gettings up and his lyings down are governed completely and solely by his own initiative No further directions are given until he asks when he can go home although such remarks as will tend to shame a slow timid patient into greater speed should not be omitted This date is determined by his demonstration while at the hospital that he is no longer invalided and the question is answered specifically by telling him that he can go home after he has been up and down two flights of stairs twice in succession The patient who can do this in the hospital as the price of going home can not in justice to himself become an invalid in the bosom of his family In particular he can not justifiably ask for breakfast in bed at home and when once up and about the house at the same time as and with the family he must to save his face and because the situation is one of his own making continue active for the rest of the day

When he has demonstrated thus that he is ready and able to go home and be active he and his immediate family are told in detail about any

permanent disabilities that have resulted from the injury A prognosis is given them relative to this phase only they are cautioned against over solicitous neighbors and it is impressed upon them that the patient has demonstrated of his own volition that he is capable of being amenable to family discipline It is then explained that except for the permanent disability already mentioned they may look upon the cranio-cerebral injury as having been completely cured and that therefore all that the patient has to do now is to build up his general condition by his own efforts until he reaches that degree of strength and activity that he had before the accident

The Third Period of Convalescence

The third period of convalescence if the foundation has been built up as described during the first two concerns the patient s general health Any modification has to do only with those rare special procedures that are called for by the presence of the permanent disabilities noted above This however does not alter from a practical point of view the truth of the preceding statement From the physician s angle the problem now is the same as that which characterizes invalidism after any serious illness such as pneumonia or a major abdominal operation except that it is simpler In handling it the patient must be made to assume again the initiative Success is not always attainable and varies directly with the degree of intelligence of the patient In any event the maximum time that should be allowed for complete return to normality within the limits of the permanent disabilities should not exceed three months from the date of leaving the hospital Patients who have had diagnoses and therapy based upon adequate demonstration of the pathology present and whose previous convalescence has been directed as above but who are not back to normal life by that time should be dismissed as permanent invalids and their families told to make arrangements to care for them as such It is only in these cases that a diagnosis of post traumatic neurosis properly can be made and only then if an exploratory transtemporal trephinement has been included among the earlier diagnostic procedures

Every physician will have his own particular methods for building up his patient s general health Provided that the underlying principle that requires the patient to assume full responsibility for his own actions and to depend upon his own initiative for his speed of recovery is recognized it makes little difference what the details of treatment are I have had most success with industrial cases however when the patient has been

allowed to put himself back to work on a part time basis before under taking a full time job again. This of course requires a type of coopera tion from the employers that the doctor may not be able to get. In general all such patients must understand in detail what their permanent disabilities are to be and they must be forced to govern their own rate of recovery by their own actions. Absolute prohibitions are as follows they must give up all alcohol for the rest of their lives they should not dive head first into water nor should they go onto high places that are not sufficiently protected to keep them from falling off in case they get faint. The danger of fainting applies also to the prohibition against diving. Obviously if this happens while under water drowning will result. Alcohol is prohibited because experience has shown that its ingestion after cerebral injury predisposes to or else will produce con vulsive seizures.

The Chronic Post Traumatic Neurotic

The patient who is commonly spoken of as having post traumatic neurosis compensation neurosis or malingering after a claimed injury to the head usually comes to the physician for relief at least a month and often years after the original injury. His complaints practically always are subjective rather than objective and his morale usually is very low. Furthermore his outlook often is prejudiced by pending litigation or some similar emotional application. Not infrequently he will have been sent by an insurance company or lawyer for an opinion as to the genuine ness of his symptoms.

Since such patients almost never go back to their original doctor for advice about their late symptomatology the physician who sees them at this later date is forced to start his investigation with a review of the original condition. He should therefore determine first of all whether or not the patient did actually receive a head injury as he claims. Head aches postural dizziness and tinnitus has been shown to occur as the only symptom in 71 64 and 45 per cent of this group and the presence of any one of these symptoms is strong presumptive evidence in favor of the patient s claim.

Confirmation may be had from the history. This should be factual and in the nature of a cross-examination. If unconsciousness amnesia before or after the accident and/or headaches after return to consciousness can be shown to have been present the doctor may conclude that the patient did in fact injure his head as claimed and may therefore be having late symptoms that are due to this old injury. A scar on the head

and appropriate x ray findings will offer further confirmation provided one can be sure that they were caused by the injury in question

This is the ultimate that can be done with an office examination An opinion that is based on such an examination and that states more than the bare fact that the patient probably did have a cranio cerebral injury as claimed and that this is an adequate cause for his present late symptoms or that the patient did not have a head injury as claimed and that therefore his late symptoms cannot be ascribed to such a cause is inaccurate and cannot be backed up by facts Further diagnostic therapeutic and prognostic details must await hospitalization of the patient

If this is consented to the investigation again must be primarily factual Ordinary hospitalization should serve to identify the presence of a previously unrecognized intercurrent physical or mental disease an expanding intracranial lesion such chronic diseases as multiple sclerosis syphilis arteriosclerosis syringomyelia pernicious anemia other blood disease disease of the kidneys local bone injury and the like Studies should include general physical and neurological examinations the making of special mental tests tests of the special senses study of the blood and urine lumbar puncture with an estimation of the intracranial pressure and chemical serologic and cytologic examinations of the cerebrospinal fluid and adequate x ray examination These all demonstrate objective facts and constitute the minimum that must be done to allow an inferential opinion as to the physical relationship between the accident in the past and the subject s symptomatology of the present If all examinations are negative the only report that can be given is to the effect that the patient at this time shows no objective evidence of disease and that he either did or did not have a previous head injury as determined from the history and that therefore his present symptoms may still be due to neurosis malingering a subdural hematoma cerebral atrophy or psychotic maladjustment

If further information is desired either for purposes of accuracy or to initiate therapy the indications for which are not already apparent the patient must submit himself to either encephalography or exploratory trans temporal trephination

Encephalography can be expected to demonstrate cortical atrophy with a high degree of accuracy solid subdural hematomas sufficiently often to be a valuable adjunct in diagnosing them and fluid subdural hematomas and encysted fluid not at all It should be noted that none of these conditions need be accompanied by any objective changes that would necessarily be demonstrable by any of the procedures discussed above Encephalography has no value as a method of treating the sub-

jective symptoms which lead to the examination Since there is a minimal but definite risk attached to the procedure, specific written permission for its performance should be obtained from the patient or his legal representatives before carrying it out

The final diagnostic procedure is trans temporal trephination This supplements encephalography and is the only way in which the presence of a fluid subdural hematoma can be recognized short of a guess It will at times also serve to establish the presence of associated non traumatic conditions that have been missed by the other examinations Fluid subdural hematomas are a more frequent cause of subjective symptoms after cranio cerebral injuries than is commonly supposed Exploratory trephination should be offered to every one of these chronic invalids for that reason alone However because it is essentially and primarily diagnostic, the offer should be qualified in such cases with the statement that no guarantee is either given or implied that the operation will afford any relief If the patient accepts it should be only with this understanding and with the clear idea that it is as likely to be a useless as it is to be a useful procedure from his point of view They can be promised however that if a subdural hematoma is found and if it is as usual fluid in type it can be treated by drainage through the same opening Furthermore they can be assured that if present and treated their chances for permanent relief of symptoms thereby are at least 3 out of 4 that the shorter the interval between the receipt of the injury and the drainage of the hematoma the greater the chance of cure and that the absence of other objective findings is of no significance since only about 1/3 of the cases that have been treated successfully in this way showed objective evidence of central nervous system disease in addition to their subjective symptoms If a subdural hematoma is present and not removed the patient will not die but will become a chronic permanent invalid and eventually may end up in an insane asylum under the mistaken diagnosis of some form of non organic psychosis

BIBLIOGRAPHY

Books

CANNON WALTER B Traumatic Shock D Appleton and Co New York 1923

COBB STANLEY A Preface to Nervous Disease William Wood and Co, Baltimore 1936

COURVILLE CYRIL B Pathology of the Central Nervous System Pacific Press Publishing Association Mountain View California 1937

CUSHING HARVEY Studies in Intracranial Physiology and Surgery Oxford Medical Publication Oxford University Press, London 19 6
DAVIDOFF LEO M and DYKE CORNELIUS G The Normal Encephalogram Lea and Febiger Philadelphia 1937
FISHBERG ARTHUR M Hypertension and Nephritis Ed 2 Lea and Febiger Philadelphia 1931
FORD FRANK R Diseases of the Nervous System in Infancy Childhood and Adolescence Chas C Thomas Baltimore 1937
LEWIS W C M A System of Physical Chemistry Longmans Green and Co New York 19 3
MERRITT H H and FREMONT-SMITH F The Cerebrospinal Fluid W B Saunders Co Philadelphia 1937
MUNRO DONALD Crani Cerebral Injuries Oxford University Press New York 1938

Physio Pathology

CASSASA CHARLES S B Multiple traumatic cerebral hemorrhages Proc N Y Path Soc N S 19 4 XXIV 101
COBB S and HUBBARD J P Cerebral hemorrhage from venous and capillary stasis report of five cases with autopsy Am Jour Med Sc 1929 CLXXVIII 693
CUSHING HARVEY Some experimental and clinical observations concerning states of increased intracranial tension Am Jour Med Sc 190 CXXIV 375
DANDY W E Experimental Hydrocephalus Ann Surg 1919 LXX 1 9
FORBES H S Cerebral circulation observation and measurement of pial vessel Arch Neurol and Psychiat 19 8 XIX 751 and succeeding papers by COBB S LENNOX W C WOLFF HAROLD G PUTMAN T J etc
FREMONT-SMITH F and KUBIE L S The relation of vascular hydrostatic pressure and osmotic pressure to the cerebro spinal fluid pressure The Proceed Assoc for Research in Nervous and Mental Disease p 104 vol VIII The Williams and Wilkins Co Baltimore 19 9
LEARY TIMOTHY Subdural hemorrhages Jour Am Med Assoc 1934 CIII 897
LECOUNT E R and APPLEBACH CARL W Pathologic anatomy of traumatic fractures of cranial bones and concomitant brain injuries Jour Am Med Assoc 19 0 LXXIV 501
MARTLAND H S Punch drunk Jour Am Med Assoc 19 8 XCI 1103
MARTLAND H S and BELING C C Traumatic cerebral hemorrhage Arch Neurol and Psychiat 19 9 XXII 1001
MUNRO D Cerebrospinal fluid pressure in the new born Jour Am Med Assoc 1928 XC 1688
MUNRO D and MERRITT H H The surgical pathology of subdural hema

tomata A study of 105 cases Arch Neurol and Psychiat 1936 XXXV 64
VANCE B M Fractures of the skull complications and causes of death review of 512 necropsies and of 61 cases studied clinically Arch Surg 19 , XIV 1023
WEED L H The absorption of cerebrospinal fluid into the venous system Am Jour Anat 1923 XXXI 191
WEED L H Experimental studies in intracranial pressure The Proceed Assoc for Research in Nervous and Mental Disease p 25 vol VIII The Williams and Wilkins Co Baltimore 19 9
WEED L H Studies on cerebro spinal fluid II The theories of drainage of cerebro spinal fluid with an analysis of the methods of investigation Jour Med Research 1914-15 XXVI 21 III The pathways of escape from the subarachnoid spaces with particular reference to the arachnoid villi Jour Med Research 1914-15 XXXI 51 IV The dual source of cerebro spinal fluid Jour Med Research 1914-15 XXXI 93
WEED L H and HUGHSON W Intracranial venous pressure Cerebrospinal fluid pressure as affected by the intravenous injection of solution of various concentrations Am Jour Physiol 1921 LVIII 101
WEISS SOMA Syncope and Related Syndromes Oxford Medicine Oxford University Press New York 1935

Diagnosis

AYER J B DAILEY M E and FREMONT-SMITH F Denis Ayer method for the quantitative estimation of protein in the cerebrospinal fluid Arch Neurol and Psychiat 1931 XXVI 1038
COLEMAN C C Chronic subdural hematomata diagnosis and treatment Am Jour Surg 1935 XXVIII 341
KOSKOFF Y D A surgical table modified for encephalography Am Jour Roent and Radium Therapy 1937 XXXVIII 93
MUNRO D Diagnosis and treatment of subdural hematomata report of 6 cases New Eng Jour Med 1934 CCX 1145
NAFFZIGER H C Subdural fluid accumulations following head injury Jour Am Med Assoc 1924 LXXXII 1751
VANCE, ROBERT G The healing of linear fractures of the skull Am Jour Roent and Radium Therapy 1936 XXXVI 744
VON STORCH T J C On the technique of encephalography with special reference to the use of the apparatus Am Jour Roent and Radium Therapy 1936 XXXV 78
VON STORCH T J C and MUNRO D Encephalography in the diagnosis of subdural hematomata New Eng Jour Med 1938 CCVIII 6

Treatment

BULLOCK L T GREGERSEN M I and KINNEY K The use of a hypertonic solution of sucrose intravenously to reduce cerebrospinal fluid pressure without secondary rise Am Jour Phys iol 1935 CXII 8
DANDY W E Diagnosis and treatment of injuries of the head Jour Am Med Assoc 1933 CI -,
FAY TEMPLE Treatment of acute and chronic cases of cerebral trauma by method of dehydration Ann Surg 1935 CI 6
FOLEY F E B Clinical uses of salt solution in conditions of increased intracranial tension Surg Gyn and Obst 19 1 XXXIII 12(
FREMONT-SMITH F and MERRITT H H Influence of variations in fluid intake in intracranial pressure in Epileptics Arch Neurol and Psych 1933 XXIX 454
GARDNER W J Recent advances in technic in neurologic surgery Surg Clinics N Am October 1937
GURDJIAN E S Studies on acute cranial and intracranial injuries Ann Surg 1933 XCVII 3
GURDJIAN E S and SHAWAN H K The management of skull fractures involving the frontal sinus Ann Surg 193 XCV 7
HOLMAN EMIL Arteriovenous aneurysm The Macmillan Co New York 1937
KENNEDY FOSTER and WORTIS S B How to treat head injuries and appraise them Jour Am Med Assoc 193 XCVIII 135
KING J E J Acute metastatic brain abscess South Surg 1936 V 407
KING J E J Brain abscess Ann Surg 193(CIII 64,
KING J E J The treatment of brain abscess associated with extracapsular necrosis and suppuration Arch Surg 193 XXXIV (31
KÖNIG Der knocherne Ersatz grosser Schädeldefecte Centralbl f Chir 1890 XXVII 497
MASSERMANN J H Effects of intravenous administration of sucrose with special reference to cerebrospinal fluid pressure Bull Johns Hopkins Hosp 1935 LVII 12
MILLES G and HURWITZ P The effects of hypertonic solutions on cerebrospinal fluid pressure with special reference to secondary rise and toxicity Arch Surg 193 XXIV 5)1
MOORE CHAS H The diagnosis and treatment of the commoner forms of cerebral trauma Jour Am Med Assoc 1937 CIX 859
MOSHER H P The wire gauze brain drain Tr Am Otol Soc 1916 XIV 10
MÜLLER Zur Frage der temporaren Schädelresection an Stelle der Trepanation Centralbl f Chir 1890 XXVII 65
MUNRO D Therapeutic value of lumbar puncture in the treatment of cranial and intracranial injury Boston Med and Surg Jour 1925 CXCIII 1187
MUNRO D The diagnosis treatment and immediate prognosis of cerebral trauma an introductory study of 1494 cases New Eng Jour Med 1934 CCX 287

MUNRO D The operative removal of retained fragments of lumbar puncture and other needles The Practitioner s Library Blumer G Editor Vol V Chapt XI p 792 D Appleton Century Co New York 1934
MUNRO D The treatment of compound fractures of the skull A study of 185 cases New Eng Jour Med 1935 CCXIII 551
MUNRO D The activity of the urinary bladder as measured by a new and inexpensive cystometer New Eng Jour Med 1936 CCXIV 617
MUNRO D The treatment of the urinary bladder in cases with injury of the spinal cord Am Jour Surg 1937 XXXVIII 120
MUNRO D The emergency care of cranio cerebral injuries Am Jour Surg 1937 XXXVIII 739
MUNRO D The surgical treatment of certain repeated explosive attacks of vertigo occurring in the absence of any demonstrable etiology —Meniere s disease A report of fourteen cases of this and other types of aural vertigo and including one case involving both vestibular nerve New Eng Jour Med 1937 CCXVI 539
MUNRO D The diagnosis and therapy of so called post traumatic neurosis following cranio cerebral injuries In Press
MUNRO D and HAHN J Tidal drainage of the urinary bladder A preliminary report of this method of treatment as applied to cord bladders with a description of the apparatus New Eng Jour Med 1935 CCXII 229
WHITE J C and WHITELAW G P Blood loss in neurosurgical operation Ann Surg 1938 CVII 287
WHITE J C SWEET W H and HURWITT E S Water balance in neuro surgical patients Ann Surg 1938 CVII 438

The New Born

BAGLEY CHAS Blood in the cerebro spinal fluid Arch Surg 1928 XVII 18
CLIFFORD STEWART H and IRVING F C Analgesia anesthesia and the new born infant Surg Gyn and Obs 1937 LXV 23
DUNHAM ETHEL C The appraisal of the new born infant U S Dept of Labor Bureau Pub 242 Washington D C 1938
EASTMAN N J Fœtal blood studies oxygen relationships of umbilical cord blood at birth Bull Johns Hopkins Hosp 1930 XLVII 221 Chemical nature of asphyxia neonatorum and its bearing on certain practical problems Bull Johns Hopkins Hosp 1932 L 39 Panel discussion on cyanosis in the new born Jour Pediatrics 1936 IX 262 Rôle of anesthesia in production of asphyxia neonatorum Am Jour Obstet and Gynec 1936 XXXI 563
LEFKOWITZ L L Extradural hemorrhage as the result of birth trauma Arch Pediat 1936 LIII 404
MUNRO D Three cases of laryngeal spasm associated with intracranial hemorrhage in the new born Ann Otol Rhin and Laryng 1925 XXXIV 677

MUNRO D Cranial and intracranial damage in the new born An end result study of 117 case Surg Gyn and Obs 1928 XLVII 62

MUNRO D Symptomatology and immediate treatment of cranial and intra cranial injury in the new born including intracranial hemorrhage New Eng Jour Med 1930 CCIII 50

MUNRO D and EUSTIS R S The diagnosis and treatment of intracranial hemorrhage in the new born Am Jour Dis Child 19 - XXIV 273

Miscellaneous

RADEMAKER G G J Reaction Labyrinthiques et Equilibre l'Ataxie Labyrinthique Masson et Cie Paris 1935

SWIFT C W Cerebrocranial injuries review of 190 cases West Jour Surg 193 XI 343

VON STORCH T J C CARMICHAEL F A and BANKS T E Factors producing lumbar cerebrospinal fluid pressure in man in the erect posture Arch Neurol and Psychiat 193 XXXVIII 1158

VON STORCH T J C and SCHWAB R S Alterations of the cerebrospinal fluid subsequent to pneumoencephalography New Eng Jour Med 1937 CCXVII 21

March 1 1939

MUNRO D The operative removal of retained fragments of lumbar puncture and other needles The Practitioner s Library Blumer G Editor, Vol V, Chapt XI p 792 D Appleton Century Co New York 1934
MUNRO D The treatment of compound fractures of the skull A study of 185 cases New Eng Jour Med 1935 CCXIII 551
MUNRO D The activity of the urinary bladder as measured by a new and in expensive cystometer New Eng Jour Med 1936 CCXIV 617
MUNRO D The treatment of the urinary bladder in cases with injury of the spinal cord Am Jour Surg 1937 XXXVIII 120
MUNRO D The emergency care of cranio cerebral injuries Am Jour Surg 1937 XXXVIII 739
MUNRO D The surgical treatment of certain repeated explosive attacks of vertigo occurring in the absence of any demonstrable etiology — Meniere s disease A report of fourteen ca es of this and other types of aural vertigo and including one case involving both vestibular nerves New Eng Jour Med 1937 CCXVI 539
MUNRO D The diagnosis and therapy of so called post traumatic neurosis following cranio cerebral injuries In Press
MUNRO D and HAHN J Tidal drainage of the urinary bladder A pre liminary report of this method of treatment as applied to cord bladders with a description of the apparatus New Eng Jour Med 1935 CCXII 229
WHITE J C and WHITFIELD G P Blood loss in neurosurgical operation Ann Surg 1938 CVII 287
WHITE J C SWEET W H and HURWITT E S Water balance in neuro surgical patients Ann Surg 1938 CVII 438

The New Born

BAGLEY CHAS Blood in the cerebro spinal fluid Arch Surg 1928 XVII 18
CLIFFORD STEWART H and IRVING F C Analgesia anesthesia and the new born infant Surg Gyn and Obs 1937 LXV 23
DUNHAM ETHEL C The appraisal of the new born infant U S Dept of Labor Bureau Pub 242 Washington D C 1938
EASTMAN N J Fœtal blood studies oxygen relationships of umbilical cord blood at birth Bull Johns Hopkins Hosp 1930 XLVII 221 Chemical nature of asphyxia neonatorum and its bearing on certain practical problems Bull Johns Hopkins Hosp 1932 L 39 Panel discussion on cyanosis in the new born Jour Pediatrics 1936 IX 262 Rôle of anesthesia in production of as phyxia neonatorum Am Jour Obstet and Gynec 1936 XXXI 563
LEFKOWITZ L L Extradural hemorrhage as the result of birth trauma Arch Pediat 1936 LIII 404
MUNRO D Three cases of laryngeal spasm associated with intracranial hemor rhage in the new born Ann Otol Rhin and Laryng 1925 XXXIV 617

CHAPTER VI

INTRACRANIAL TUMORS

By Wilder Penfield and Donald McEachern

Table of Contents

CHAPTER VI

INTRACRANIAL TUMORS

By Wilder Penfield and Donald McEachern

Table of Contents

Introduction

In the past the diagnosis of "brain tumor" has had a connotation as dreadful for the laity as that of "cancer" and "galloping consumption" Members of the medical profession also have shown a tendency to adopt an attitude of resignation this attitude is no longer justified Some brain tumors it is true give a hopeless prognosis but other varieties are completely remediable Handbook descriptions which were formerly expressed in vague generalities must be replaced by concise detailed descriptions of tumor types localizations and syndromes

The general practitioner must be alert to the fact that the child who has been for a period of months cross and unsteady on his feet may have a cerebellar tumor the adult who is deaf on one side and deviates to that side in walking may well have a remediable acoustic tumor and the middle aged man who has very rapidly increasing mental dullness and headache quite possibly has an irremediable glioblastoma

Specialization has made possible great therapeutic advances Pneumography as a preliminary to operation has substituted certainty of localization for presumptive diagnosis But this has made the neurologist's counsel all the more important and instruction of the practitioner all the more urgent It has converted the patella hammer and the ophthalmoscope into effective instruments that point less often to interesting anomalies and more often to constructive therapy

Intracranial Alterations Produced by Expanding Lesions

Obviously a tumor growing within the skull must produce increased intracranial pressure because of the fact that the skull is a closed box The expanding lesion compresses the brain and disturbs the circulation of cerebrospinal fluid and of blood through and about the brain The mechanism of these disturbances is common to all types of tumor and is now described in brief outline This mechanism must be studied in order to understand the effects of tumor growth and the ventricular displacement as shown by ventriculography

Circulation of Cerebrospinal Fluid

Under normal conditions cerebrospinal fluid is formed within the choroid plexuses in the lateral ventricles of the brain It flows into the third ventricle and down the aqueduct of Sylvius into the fourth ventricle (Fig 1) and out into the cisterna magna and basal subarachnoid

of Galen or of the lateral sinus may cause congestion of the choroid plexus and increased formation of cerebrospinal fluid but they point out that increase of intracranial pressure does not result unless absorption is impaired also

In general the all important regulator of the cerebrospinal fluid pressure is the rate of absorption of the fluid Consequently the pres

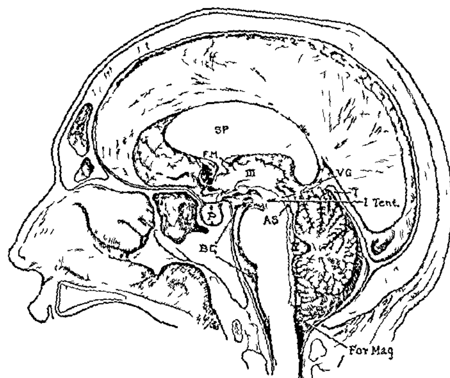


FIG 2 Sagittal section through skull and longitudinal sinus (S) to show relation of falx and tentorium (T) to right half of brain SP septum pellucidum FM right foramen of Monro III third ventricle AS aqueduct of Sylvius IV fourth ventricle CM cisterna magna BC cisterna basalis the upper portion being the cisterna interpeduncularis P pituitary gland VG great vein of Galen I Tent dotted outline of incisura of tentorium beyond brain stem For Mag foramen Magnum

sure may be increased by obstruction to the circulation of the fluid at any point between its origin in the ventricles and its absorption in the subarachnoid space over the vault

cisternæ (C and BC Fig 2) From the cisterna magna some fluid passes outward over the cerebellum to be absorbed into the subarachnoid veins there but most of it passes forward and upward through the basal cisternæ to the interpeduncular cisterna from which it flows into the fissures of Sylvius and bathes the surface of the cerebral hemispheres There it

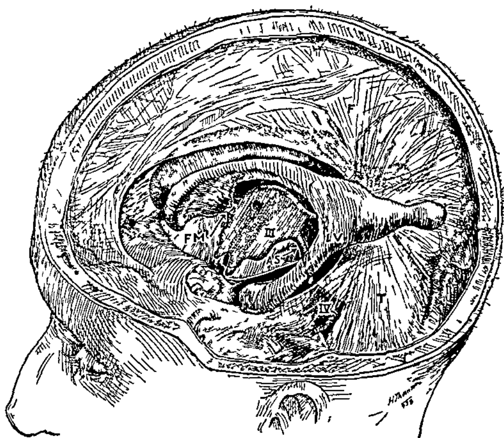


FIG 1 Schematic representation of the ventricles in relation to falx (F) and tentorium (T) FM foramen of Monro III third ventricle AS aqueduct of Sylvius LV lateral ventricle IV fourth ventricle

is reabsorbed into the blood stream through the walls of the veins within the subarachnoid space and into the dural sinuses through the pacchionian granulations

Increase of intracranial pressure results whenever formation of cerebrospinal fluid exceeds the rate of its absorption Under normal conditions an increase of fluid pressure results in an increased rate of absorption Mortensen and Weed[77] have shown that compression of the vein

of complete obstruction nevertheless tends to dilate the ventricles Less dilatation takes place on the ipsilateral side (Fig 3) for the pressure of the tumor within that hemisphere resists ventricular dilatation more effectively than the somewhat lower pressure within the other hemisphere

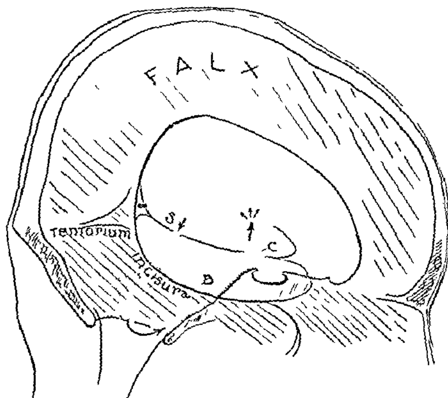


Fig 3 The dural partitions within the skull to show how the aqueduct of Sylvius (S) carries fluid down through the incisura tentorii and how the cisterna basalis (B) brings the fluid back to the cisterna interpeduncularis (C) whence it is distributed over the surface of the cerebral hemispheres to be absorbed

As expansion continues the structures of the hemisphere which is being compressed begin to herniate under the falx into the opposite half of the cranial chamber (Figs 18 and 19) The aqueduct now is pressed upon more severely and the intraventricular pressure mounts rapidly Dilatation of the opposite ventricle which has been gradual up to this point progresses at increased pace and signs of increased intracranial pressure become acute

Ventricular Dilatation

A relatively small expanding lesion within the cerebellum or in the cerebello pontile angle shuts off escape of cerebrospinal fluid down the aqueduct of Sylvius (AS Fig 1) and consequently the pressure within the ventricles which lie above rises to a figure which may be as high as from 400 to 700 mm of water This high pressure produces hydrocephalic ventricular dilatation and generalized increase of intracranial pressure Thus a small tumor in this strategic situation produces earlier pressure increase than would the same sized lesion above the tentorium Curiously enough however an infiltrating neoplasm of the pons and medulla oblongata is rather slow to shut off the fluid escape

Obviously an expanding lesion in the vicinity of the third ventricle may produce dilatation of the lateral ventricles and such a lesion placed close to one foramen of Monro may occlude it and cause dilatation of the corresponding lateral ventricle

Effect upon the Brain of an Expanding Lesion

A slowly expanding lesion within or upon one cerebral hemisphere can displace the brain a considerable distance with little increase of intracranial pressure and with little disturbance of function at first Slowly increasing pressure upon brain whether from tumor or ventricle causes it to decrease in volume as though it melted with remarkably little disturbance of function This decrease in tissue volume takes place chiefly in the white matter and collateral branches are probably sacrificed while essential axones are preserved[99]

An expanding lesion placed anywhere in one cerebral hemisphere in such a position as not to obstruct a ventricle directly eventually will increase intracranial pressure but not equally so, throughout the cranial cavity The pressure upon or within the affected hemisphere exceeds that of the opposite hemisphere or the cerebellum because of the resistance offered by the cerebral tissue and by the falx and tentorium The falx is quite rigid enough to subdivide the cranial box into two lateral compartments and the tentorium still more effectively separates off the posterior fossa of the skull into a third compartment (Figs 3 and 5)

But the pressure within the affected hemisphere ha a distant effect upon the aqueduct of Sylvius which lies within the incisura of the tentorium (Fig 4) It tends to collapse the aqueduct so that cerebrospinal fluid can only escape down this channel when forced by increased pressure in the ventricles This back pressure although not as great as in the case

of complete obstruction nevertheless tends to dilate the ventricles Less dilatation takes place on the ipsilateral side (Fig 5) for the pressure of the tumor within that hemisphere resists ventricular dilatation more effectively than the somewhat lower pressure within the other hemisphere

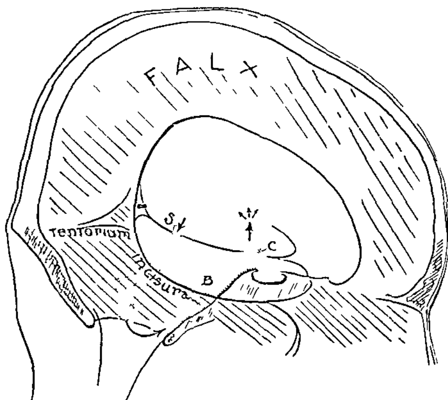


FIG 3 The dural partitions within the skull to show how the aqueduct of Sylvius (S) carries fluid down through the incisura tentorii and how the cisterna basalis (B) brings the fluid back to the cisterna interpeduncularis (C) whence it is distributed over the surface of the cerebral hemispheres to be absorbed

As expansion continues the structures of the hemisphere which is being compressed begin to herniate under the falx into the opposite half of the cranial chamber (Figs 18 and 19) The aqueduct now is pressed upon more severely and the intraventricular pressure mounts rapidly Dilatation of the opposite ventricle which has been gradual up to this point progresses at increased pace and signs of increased intracranial pressure become acute

Terminal Effects of Increased Pressure

If the tumor expands rapidly the brain does not melt away It is compressed with consequent loss of function and events lead swiftly to death Slow expansion may be converted suddenly into rapid expansion

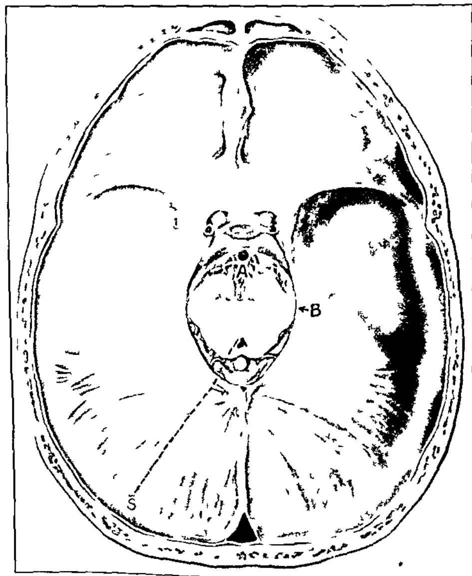


FIG 4 Drawing of the base of the skull with the tentorium in place to show the relation of midbrain aqueduct of Sylvius (S) and cisterna interpeduncularis (A) to the incisura tentorii (B) (After Penfield 1935)

by hemorrhage into the substance of a tumor or by rapid cyst formation. But whether the evolution is slow or fast, the following phenomena appear eventually. The high pressure compresses the intracranial veins and thus impedes the outflow of blood from the brain. The resulting increase in venous pressure allows reabsorption of fluid into the veins only at a higher fluid pressure. In addition, the increase of venous pressure in the choroid

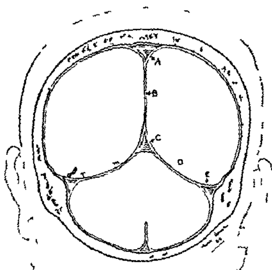


FIG. 5. Schematic frontal transection of cranium to show falx, tentorium and dural sinuses. (After Penfield, 1934.)

plexus results in more forceful formation of cerebrospinal fluid and thus establishes a vicious circle of mounting pressure.

The brain then tends to be forced from the cranial cavity by the only existing outlets, the incisura of the tentorium (Figs. 2 and 4) and the foramen magnum (Fig. 2). Herniation through the incisura produces ischemia of the mesencephalon, which results in coma and paralysis of the third cranial nerve. Herniation of the cerebellum downward into the foramen magnum may also occur, especially if the expanding lesion is situated in the posterior fossa, and this produces ischemia of the medulla oblongata, resulting in arrest of respiration preceded by Cheyne-Stokes breathing. For clinical signs of compression the reader is referred to the Section further along on Clinical Evidence of Increased Intracranial Pressure. Obviously, cisternal puncture is very dangerous, and lumbar puncture, if done recklessly, may precipitate bulbar paralysis by withdrawing the support exerted by the cerebrospinal fluid pressure

below Even in the absence of such precipitating factors respiratory arrest may occur with startling suddenness in patients with high intra cranial pressure

Increased Intracranial Pressure from other Causes than Tumor

Although brain tumor is the most frequent cause of a continuing in crease of intracranial pressure other causes must be recognized These include premature clo ure of the sutures occurring in childhood before the growth of the brain has ceased (oxycephaly) thickening of the inner surface of the skull as in Paget s disease subdural hematoma pacchy meningitis hemorrhagica interna brain abscess internal hydrocephalus due to adhesive closure of the subarachnoid spaces or to chronic meningi tis tuberculous syphilitic etc or congenital malformations etc So called otitic hydrocephalus which in reality usually means a subdural effusion of fluid secondary to an inflammatory process in the mastoid may also produce an increase of pressure without localizing signs Furthermore a continuing increase of intracranial pressure may occur though rarely as a result of cerebral edema in encephalitis lethargica Schilder s encepha litis lead intoxication and cerebral trauma

Effect of Hydration and Dehydration

Weed and McKibben[16] were the first to show that changes in the osmotic pressure of the blood greatly modify the bulk of the brain and the pressure of cerebrospinal fluid Intravenous injection of a hypotonic solution e g distilled water causes increased formation and decreased absorption of cerebrospinal fluid the brain swells and intracranial pres sure rises Conversely injection of hypertonic solution e g 15 per cent sodium chloride solution causes the brain to shrink and lowers the intra cranial pressure These factors are of great importance in the manage ment of increased intracranial pressure Measures leading to hydration of the blood e g large amounts of water by mouth hypotonic solutions by rectum are contraindicated Measures leading to dehydration e g saline cathartics administration of hypertonic solutions intravenously or by rectum are known to benefit the symptoms of increased intracranial pressure

Magnesium sulphate may be given every four hours by mouth ℥iss (45 gm) of the crystals in ℥viii (240 c c) of water or by rectum ℥iii (90 gm) of the crystals in ℥vi (180 gm) of water until the intracranial pressure has been lowered effectively Hypertonic solutions introduced intravenously

act more quickly Glucose 50 to 100 c c of 50 per cent solution is superior to hypertonic sodium chloride in producing a sustained several hours fall of intracranial pressure with less tendency to a subsequent rise exceeding the initial pressure Results seem to indicate that the use of sucrose as suggested by Bullock Gregersen and Kinney[1] is even more effective for the control of increased intracranial pressure One hundred to 200 c c of 50 per cent solution may be given intravenously Sucrose is excreted unchanged in the urine and therefore has no nutritive value

The above measures have but a temporary effect and for this reason are used chiefly in cases of brain tumor as part of the preoperative preparation and postoperative treatment

Cerebrospinal Fluid Alterations Produced by Brain Tumor

Examination of the cerebrospinal fluid is at times helpful in the diagnosis and even in the localization of intracranial tumors The subject is dealt with in general elsewhere (Vol VI Chapt XL) and we refer here only to specific points The reader also may amplify his information on this subject by reference to Greenfield[6] and to the exhaustive studies of Hare[38] and Fremont Smith[39] who respectively have reported their findings in 186 and 164 cases of verified cerebral tumors

Punctures

The fluid usually is drawn from the lumbar region and less commonly from the cisterna magna or lateral ventricle The fluids obtained from these regions differ somewhat even in the normal individual In case of tumor they may differ widely in pressure and constitution and these differences may assist in determining both the location and type of tumor

Lumbar puncture is a hazardous procedure in the presence of increased intracranial pressure due to tumor and should be omitted unless the evidence is essential Although the danger may be exaggerated the greatest caution should be employed especially if a neoplasm of the posterior fossa is suspected In this case lumbar puncture should be omitted and fluid obtained from the ventricle if at all For lumbar puncture a small bore needle should be used and fluid not exceeding a few cubic centimeters should be removed drop by drop with the patient in the horizontal position If signs of respiratory embarrassment or significant changes in blood pressure or pulse rate occur the procedure should be terminated

Combined ventricular and lumbar puncture as recommended by Fremont Smith and Hodgson[51] is safer than lumbar puncture in cases

with high intracranial pressure and yields more information Ventricular puncture alone probably is still safer but it should be remembered that syphilis cannot be excluded by examination of ventricular fluid which may prove quite normal, while the lumbar fluid shows the changes characteristic of syphilis

Abnormalities of cerebrospinal fluid in the presence of cerebral tumor are related to a number of factors These include the proximity of neoplasm to ventricle or leptomeninges its size type and vascularity as well as the amount of hemorrhage and degeneration associated with it

Cerebrospinal Fluid Pressure

The normal pressure for the adult in the lateral recumbent position ranges between 120 and 170 mm of cerebrospinal fluid It is slightly less than this in the child Pressure of over 200 mm generally is looked upon as abnormal Pressure of 500 mm or higher sometimes is found in cases of intracranial tumor The pressure was higher than normal in over 70 per cent of Fremont Smith s cases of brain tumor

A normal pressure in no way excludes tumor A persistently elevated pressure or one that is rising as determined by repeated punctures is strongly in favor of tumor Increased pressure may be present however for several months before the appearance of papilledema It should be remembered that vomiting diarrhœa and other causes of dehydration may lower an otherwise high pressure and conversely procedures leading to hydration may elevate it Both ether and morphine tend to elevate the pressure

Measurement of pressure with the patient in the sitting posture as before encephalography is unsatisfactory In this position the fluid in a glass manometer (Ayer) usually rises to about 10 cm below the top of the patient s head (Fig 13) Anything above this level may be considered abnormally high

Occasionally lumbar puncture pressure may be within normal limits although the intracranial pressure actually is high This may be due to blockage of the downward flow of fluid and would indicate that withdrawal of fluid may be dangerous Furthermore a slowly expanding lesion such as a slowly growing tumor or subdural hematoma may allow temporary readjustment of the whole brain so that the pressure may be normal temporarily

It has been pointed out elsewhere in this chapter that there are many causes of increased pressure other than intracranial tumor e g meningitis subarachnoid hemorrhage vascular hypertension especially when

associated with uremia, oxycephaly, etc. Elevation of cerebrospinal fluid pressure must therefore be evaluated along with other clinical evidence.

Protein Content

Quantitative determination of the total protein content of the cerebrospinal fluid is of great importance in cases of suspected brain tumor. The upper limits of normal are 45 mgm. per cent for lumbar fluid, 25 mgm. per cent for cisternal fluid and 15 mgm. per cent for fluid from the lateral ventricle. Although qualitative tests of globulin (Pandy) frequently parallel the increase of total proteins, they are but a rough guide. In Hare's series the lumbar fluid showed an elevation of protein in 61 per cent of cases of meningeal fibroblastoma and in 65 per cent of cases of glioblastoma multiforme. All cases of perineurial fibroblastoma of the VIII nerve and other tumors of the cerebello-pontine angle showed an increased protein. An increase occurred in 35 per cent of astrocytoma cases when the tumor was above the tentorium but in no instances when it was subtentorial. Fremont-Smith's study showed that the lumbar fluid protein is above normal in 70 per cent of all cases of brain tumor. It is higher than 100 mgm. per cent in about 30 per cent, but the value rarely exceeds 500 mgm. per cent.

It is generally considered that the increased protein is due to transudation from blood vessels or from degenerating areas in the tumor or possibly from surrounding areas of edema. An increase therefore is likely to occur if the tumor is especially vascular, if it is rapidly growing and malignant, and if it is near to or invades the ventricular system. In tumors of the cerebello-pontine angle the increase of protein probably is due in part to block and stagnation of fluid in the lumbar sac and also to seepage from congested vessels in or around the tumor. A tumor in the cerebral hemisphere seldom causes an increase in protein unless it lies deep and invades the ventricular system.

Merritt and Fremont-Smith have discussed the relation of the protein content of ventricular fluid to that of the lumbar fluid. If the lumbar fluid protein is normal, that in the lateral ventricles also is normal. A tumor invading one lateral ventricle causes an increase of protein in the fluid from that ventricle while fluid from the opposite ventricle is normal. Tumor of the corpus callosum, of the third ventricle or multiple metastatic tumors may cause high protein in the fluid from both lateral ventricles. In posterior fossa tumors the fluid from both lateral ventricles is normal.

Increase of protein in the cerebrospinal fluid is, of course, a common

finding in many conditions other than tumor which affect the central nervous system Bleeding into the subarachnoid space may of itself cause an elevation of protein due to dilution of blood proteins in the cerebrospinal fluid For each 1 000 red blood cells per cu mm of cerebrospinal fluid there is an increase of about 1 mgm per cent of protein A protein content out of all proportion to the amount of blood present might be evidence of tumor Xanthochromia is said to occur in about 15 per cent of tumor cases and usually is associated with considerable increase of protein although occasionally it may result from blood pigment derived from extravasations of blood too small to elevate the protein

Cells in the Fluid

Increase of leucocytes in the cerebrospinal fluid is rare in cases of cerebral neoplasm Only 9 per cent of Hare s cases showed a cell count above 10 per cu mm Counts up to several thousand have been described however and when acute degeneration or hemorrhage takes place within an infiltrating tumor large numbers of polymorphonuclear leucocytes may be found in the spinal fluid Cerebral abscess occasionally is associated with pleocytosis as are rare granulomata

Red blood cells usually are not present In rare instances extravasation of blood may occur in amounts varying from microscopic to massive hemorrhage In the latter event the picture may be indistinguishable from that of spontaneous subarachnoid hemorrhage due to simple vascular lesions Russel and Kershman[107] have described sudden gross subarachnoid hemorrhage in three cases of cerebral tumor

When cells are present in the fluid they should be studied carefully and if there is any doubt as to their nature the fluid should be centrifuged and the sediment embedded in celloidin for metastasis occurs through the spinal fluid in certain gliomas as described in the section on Morbid Anatomy and we have made the diagnosis in this manner

Other Examinations

The Wassermann reaction of the blood and if safe of the lumbar fluid should be determined in all cases of suspected brain tumor It is not only necessary to exclude syphilis as a cause of symptoms but it is also necessary to remember that a neoplasm and syphilis may coexist

Other types of examination are of little or no value There is no characteristic colloidal gold curve and when real precipitation occurs in

about 35 per cent of cases usually it is in the middle zone and due to the high protein content of the fluid The sugar and chloride value usually are normal although occasionally they are altered due to general metabolic upset e g hyperglycemia lowered plasma chloride due to vomiting etc

Clinical Evidence of Increased Intracranial Pressure

It is convenient to divide the evidences of intracranial tumor into those that are general and attributable to increased intracranial pressure and those that are focal and produced by the local effect of the growth The first group is treated in this section and the second group in the next section that on Localization Despite the improved x ray methods for recognizing tumors in the earlier stages it must be confessed that the clinical diagnosis is made in many instances only after the onset of increased intracranial pressure about 70 per cent Occasionally the intracranial pressure remains normal even when a large tumor is present This may occur if the expansion of the tumor has been slow enough to allow complete readjustment of the brain to its presence

Headache vomiting and papilledema are the cardinal signs of generalized increase of intracranial pressure In a series of cerebral tumors reported by Brain[1] headache occurred in 88 per cent papilledema in 75 per cent and vomiting in 65 per cent All three manifestations occurred together in 60 per cent of the cases To this triad should be added other signs particularly strabismus as will be described below

Headache

Simple increase of intracranial pressure usually gives rise to frontal headache although an expanding lesion in the posterior fossa of the skull may cause reference of the ache into the occipital and posterior cervical regions The headache usually is dull often throbbing and made worse by exertion and stooping In young children often there is no complaint of headache but the parents are apt to observe that the child has become bad tempered Severe headache which comes on very suddenly and may be precipitated or relieved by change of head posture sometimes is produced by a movable or pedunculated tumor within one ventricle which blocks one foramen of Monro or the aqueduct of Sylvius intermittently by ball valve action

Certain other types of headache must be differentiated from the above *Migraine* which is associated at times with vomiting is more

apt to be episodic and has certain characteristic features It is related to emotional stress and in women usually is related to the menstrual cycle It is often familial and first makes its appearance at the time of puberty An attack is apt to be ushered in with a sense of fatigue and with visual phenomena such as lights and figures before the eyes Photophobia may appear during an attack The localization usually is behind one eye but it may be bilateral Ergotamine tartrate administered at the onset usually succeeds in aborting an attack if the condition is true migraine

Headaches due to *eye strain* ordinarily are localized in or near the eyes They are apt to be made worse by reading and especially by watching cinematographic performances A *post traumatic* headache usually is more constant and more influenced by posture The localization of post traumatic headache may be at any point but this point does not vary in the same patient The character of the ache is dull pressing or pounding with an occasional stabbing or sticking pain Such headaches usually are associated with recurring bouts of dizziness often brought on by change of head posture

The headache produced by *vascular hypertension* usually is throbbing in character and grows worse as the day proceeds Patients often complain of feeling a helmet like pressure upon the head which extends down the back of the neck Headache due to disturbance within the *nasal sinuses* usually is referred directly to the region of the involved sinus cavity with a frequent tendency to radiate lateralward to the mastoid region of one side and the neck on that side Pain from the sphenoid sinus or ethmoids may be bilateral and may simulate the headache of increased intracranial pressure

Vomiting

Often this is a late symptom It probably indicates some anemia of the vagal centers in the medulla oblongata due to pressure in the vicinity of the foramen magnum In children vomiting often is the first symptom and may continue for many months before other symptoms appear Hiccoughs may indicate a similar disturbance

Papilledema

Papilledema or choking of the optic papilla is the most reliable objective evidence of increased intracranial pressure in the adult Every physician should equip himself with an adequate ophthalmoscope The

patient's pupils should be dilated for those with less experience or when the pupils are contracted. In doubtful cases repeated examinations should be made to note change or progression. In the earliest stage of papilledema there may be only a slight blurring of the nasal margins of the optic discs together with darkening and engorgement of the retinal veins.

As the condition progresses the optic disc becomes pink and the haziness of the margins extends from the nasal and upper margins all the way round. The physiological cup fills in and the whole nerve head swells and bulges forward from 1 to 6 diopters or even more. White shining exudate appears on and about the nerve head as the condition progresses. Sometimes it is guided by the nerve fibrils and converges from the papilla to the macula or it follows vessels out from the nerve head. Small punctate hemorrhages appear on and about the papilla and larger hemorrhages and patches of cottony white exudate may occur in the surrounding area. Exudate may spread in radiating fashion about the macula and form the typical macular fan.

Papilledema almost always results in blindness if allowed to continue long enough, 3 months to 2 years. Loss of vision due to the secondary optic atrophy that follows papilledema in general is less recoverable than loss of vision which is associated with the primary optic atrophy due to direct pressure upon optic nerves or tracts. Only a few weeks may elapse between the first disturbance of vision by papilledema and its complete loss even though the papilledema had been of long standing. Furthermore if visual acuity becomes too much reduced complete blindness may ensue even if the intracranial pressure is relieved at this late date.

Many a patient has been cured of the cause of his increased intracranial pressure by operation but has remained permanently blind only because of the failure of his physician to recognize the existence or the urgent significance of papilledema.

With the onset of diminution of visual acuity due to papilledema there occurs progressive constriction of the peripheral visual fields and increase in size of the blind spots. Rarely perfect vision may be maintained for a short time in the presence of a high degree of papilledema and similarly if decreased vision is of short duration when the pressure is relieved there may be return to perfect vision. Fleeting periods of diminished vision or complete blindness may occur and have been spoken of by patients as "black outs." This transient amblyopia perhaps is due to passing changes in the retinal circulation.

The papilledema is sometimes greater in the eye on the same side as the tumor and the swelling of the disc sometimes appears first in that

apt to be episodic and has certain characteristic features It is related to emotional stress and in women usually is related to the menstrual cycle It is often familial and first makes its appearance at the time of puberty An attack is apt to be ushered in with a sense of fatigue and with visual phenomena such as lights and figures before the eyes Photophobia may appear during an attack The localization usually is behind one eye but it may be bilateral Ergotamine tartrate administered at the onset usually succeeds in aborting an attack if the condition is true migraine

Headaches due to *eye strain* ordinarily are localized in or near the eyes They are apt to be made worse by reading and especially by watching cinematographic performances A *post traumatic* headache usually is more constant and more influenced by posture The localization of post traumatic headache may be at any point but this point does not vary in the same patient The character of the ache is dull pressing or pounding with an occasional stabbing or sticking pain Such headaches usually are associated with recurring bouts of dizziness often brought on by change of head posture

The headache produced by *vascular hypertension* usually is throbbing in character and grows worse as the day proceeds Patients often complain of feeling a helmet like pressure upon the head which extends down the back of the neck Headache due to disturbance within the *nasal sinuses* usually is referred directly to the region of the involved sinus cavity with a frequent tendency to radiate lateralward to the mastoid region of one side and the neck on that side Pain from the sphenoid sinus or ethmoids may be bilateral and may simulate the headache of increased intracranial pressure

Vomiting

Often this is a late symptom It probably indicates some anemia of the vagal centers in the medulla oblongata due to pressure in the vicinity of the foramen magnum In children vomiting often is the first symptom and may continue for many months before other symptoms appear Hiccoughs may indicate a similar disturbance

Papilledema

Papilledema or choking of the optic papilla is the most reliable objective evidence of increased intracranial pressure in the adult Every physician should equip himself with an adequate ophthalmoscope The

ing value The long course of this nerve on the base of the skull seems to expose it to injury by compression Dilatation of one pupil and strabismus due to paralysis of the oculomotor nerve may indicate a much graver degree of pressure This may occur when the temporal lobe begins to herniate through the incisura of the tentorium and the mesencephalon thus is strangulated there

Enlargement of Head

Enlargement of the head with wide separation of the sutures and increase in the size of the fontanelle occurs in infants as an unmistakable evidence of increased intracranial pressure During childhood and even up to puberty the sutures may separate as the result of long continued high pressure This produces a cracked pot sound when the skull is percussed especially over the suture line itself and it has no reference to the ventricular cavities within the brain Moderate exophthalmos usually bilateral and enlargement of veins of the forehead temples and scalp may occur both in children and adults

Convolutional Atrophy of the Skull

Increased convolutional markings upon the under surface of the skull as shown by roentgenography may be produced by long continued pressure of the cerebral convolutions outward upon the bone It must be remembered however that during childhood the normal increase in size of the skull is brought about by yielding to growth of the brain and consequently convolutional atrophy of the skull is a normal finding during the period of growth In adults it usually signifies abnormally increased pressure while in childhood a greater degree than normal has the same significance

Thinning of the Clinoid Processes

Roentgenography also gives evidence of long continued increased pressure by thinning of the clinoid processes and a tendency for the sella turcica to become shallower

Signs of Acute Compression

In this discussion of the signs of increased intracranial pressure no mention has been made as yet of the changes produced by sudden increase

eye a lateralization which has been reported even in cases of subtentorial tumor But this relationship certainly is not to be relied upon as a guide to localization A tumor on the under surface of one frontal lobe may compress directly the optic nerve on that side and thus prevent papilledema by closing the subarachnoid sheath about the nerve Consequently it produces primary optic atrophy on that side whereas papilledema occurs in the opposite eye This phenomenon Foster Kennedy syndrome is of real localizing value indicating a tumor on the side of the optic atrophy

The primary histological change which occurs in optic nerve and nerve head is actual swelling of the neurofibrils themselves[19] Two factors at least may operate in the production of this change Increased pressure within the subarachnoid sheath of the optic nerve and obstruction of the central vein of the retina as it traverses the subarachnoid space thus causing venous congestion exudation and hemorrhage of the disc and retina The fact that direct pressure upon the optic nerve prevents papilledema suggests that back pressure of the spinal fluid within the sheath about the nerve is an essential element in the production of edema of the nerve head

If papilledema is allowed to run its full course the edema eventually is replaced by degeneration of the nerve fibers and the nerve head becomes white But even later there may be traces of the exudate that was present formerly now healed and this indicates to the practised ophthalmologist that the condition is one of secondary optic atrophy i e secondary to papilledema Direct pressure upon an optic nerve also produces blindness and atrophy of the nerve head but this is not preceded by edema and the scarring about the vessels therefore is absent This is primary optic atrophy

Papilledema secondary to increased pressure within the cranial cavity must be distinguished from the neuroretinitis associated with renal insufficiency and arterial hypertension In the latter case the exudate and hemorrhages tend to appear widely over the retina instead of focusing upon the papilla as in papilledema Also in this form of neuroretinitis the hemorrhages and exudate often are greater in the presence of a small amount of elevation of the nerve head than they are in the choked disc of increased pressure

Strabismus

Strabismus due to paralysis of one or both abducens nerves is a frequent manifestation of increased intracranial pressure without localiz

LOCALIZATION

Head Pain

Head pain may serve to localize a brain tumor occasionally A superficial tumor which impinges upon a sensitive area of the dura or a dural sinus may cause local pain This occurs most often in the case of meningeal fibroblastoma where an occasional sharp sticking pain may indicate the site of attachment to the dura

The brain usually is insensitive as are all the smaller cerebral vessels Only the large arteries that arise in the circle of Willis and occasionally large veins as they enter the longitudinal sinus are capable of giving rise to pain The convexity of the dura is sensitive only where the middle meningeal arteries run and the pain due to involvement of such areas is accurately localized All of the dural sinuses are sensitive and the pain is sometimes local sometimes referred Pressure upon or stretching of the right lateral wall of the longitudinal sinus (A Fig 5) causes pain on the right side of the head and vice versa If the mid portion is involved the ache often is referred to ipsilateral temple and face Pain arising from the posterior part of the sinus is referred forward to the frontal region of the same side Pressure downward upon the transverse sinus or the tentorium (at F or D Fig 5) produces pain behind the ipsilateral eye Pressure upward upon the transverse sinus from below gives pain that radiates downward Thus the semi rigid dural sinuses are sensitive to pressure upon their drum like walls and traction upon those walls by pressure on one side of falx or tentorium as at B or D Fig 5 stretches the sinuses and also produces pain This explains the mechanism and distribution of pressure headache whether localized or generalized[37]

Consequently the frontal headache of generalized increase of intracranial pressure above the tentorium is caused by the combined pressure upon the upper walls of the transverse sinuses and both walls of the longitudinal sinus When the increase of pressure is chiefly in the posterior fossa the ache is referred to occiput and back of neck because of the tension of the under wall of the horizontal sinuses If a tumor impinges upon the gasserian ganglion in one middle fossa sharp shooting pain is produced in the face on that side and some paresthesia

Epileptiform Seizures

Of a series of 450 intracranial tumors studied by Penfield and Tarlov a study to be published shortly 69 per cent were in a supratentorial

in that pressure These signs indicate acute danger in cases of brain tumor but do not continue for any long period of time

(*a*) Slowing of the pulse down to 60 or even 40 is a reliable sign of acute increase of intracranial pressure The pulse is pounding in character because with this slowing usually there is

(*b*) a rising systolic and falling diastolic pressure which produces a large pulse pressure These two phenomena of slowing pulse and rising blood pressure apparently are due to vagal stimulation resulting from inadequate circulation in the medulla oblongata

(*c*) Cheyne Stokes breathing may occur and is characterized by periodic slowing or even arrest of respiration General alertness and spontaneous movements usually decrease during each apnoeic period This evidently indicates a phasic variation in blood flow through the medulla oblongata the survival of which now is seriously threatened The intracranial pressure now has become so high that in spite of increased systemic arterial pressure capillary flow through the bulb is hardly possible and there results an ebb and flow in the activity of the respiratory center There is apt to be at this stage herniation of the cerebellum down into the foramen magnum (Fig 2)

Difficulty in swallowing accumulation of thick mucus in the pharynx regurgitation of fluids through the nose and dysarthria sometimes occur as earlier evidences of impending bulbar paralysis

(*d*) Drowsiness and stupor deepening into coma are associated with terminal herniation through the incisura tentorii and foramen magnum as described previously in the second section of this chapter but this deepening stupor seems to be directly associated with the anemia of the midbrain (Fig 4) Attention has been called to the trick of repeatedly rubbing the nose with the hand which patients in this condition sometimes exhibit

(*e*) Dilatation of the pupil and external strabismus due to paralysis of one or both oculomotor nerves indicate that the midbrain has reached its limit of metabolic embarrassment just as the permanent apnœa which follows Cheyne Stokes breathing signalizes the advent of paralysis of the bulb

After these final signs appear decompressive operation or ventricular puncture together with artificial respiration may prolong life for a few hours but it is almost invariably too late to restore the damaged ganglion cells Complete ischemia lasting but a few minutes leads to irreparable loss of function

essential difference Anyone having the opportunity to observe attacks should be schooled to note and to describe them with the utmost accuracy Failure to observe the early pattern of an attack is a great opportunity lost The importance of this should be taught to every physician interne nurse and relative A detailed account of the patient s

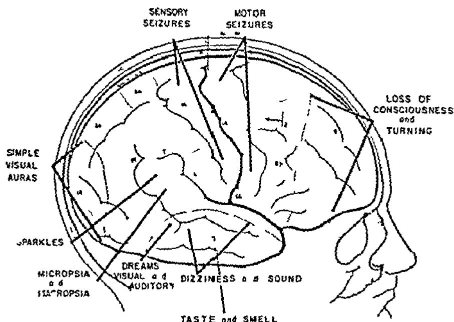


FIG 6 Chart of common initial phenomena in epileptic seizures arising in different areas of the brain The leading lines indicate general and not punctate localization For the details of motor and sensory patterns see figures [illegible])

first sensation or aura should be obtained Movement of the eyes head face trunk and isolated movements of the limbs expression of the face flushing or pallor tasting and smacking movements of the tongue and lips should be noted

Duration of the aura the time taken for the march of symptoms and the time occupied by the entire seizure are all points of importance The frequency and severity of seizures should be charted and a note made of any factor tending to precipitate or to abort attacks noises bright lights excitement sensory stimuli food In like manner factors tending to increase the number or the severity of attacks should be recorded such as — menstrual cycle diet relation to meals and to sleep effect of fatigue alcohol Objective physical signs such as muscular weakness

position Of the supratentorial neoplasms there was a history of seizures in 55 per cent Some of these attacks could be recognized easily as focal In others the pattern was not so easily analyzed

Bravais in 1827 was the first to describe focal motor convulsions of limited range and deliberate onset but it remained for Hughlings Jackson to delineate their pattern and to point out the common relationship to focal disease of the brain The clinician however is still apt to regard Jacksonian seizures as purely motor phenomena On the contrary as Jackson himself perceived such explosions of activity may begin in or be limited to many different functional areas of the brain Thus the attack may be characterized by sensory motor or mental phenomena A focal attack may last but a few seconds and remain exquisitely localized to a single part of the brain Depending upon the cortical area involved there may be movements of a single digit numbness or tingling similarly delimited sudden flashes of light auditory olfactory or other phenomena More often there is a spread of excitation in the brain from the focus originally involved and thus a march of the symptoms occurs the pattern of its expression being governed by the map of function of the cerebral cortex It is important to recognize that this spread is over the surface of the cortex rather than along association tracts Thus movement or numbness of one foot may spread to leg thigh abdomen, thorax shoulder hand and face (Figs 28 and 29)

Details of epileptic seizures arising in different areas will be found under syndromes as described in a later section In general as shown in Fig 6 attacks ushered in by a visual aura usually are due to a lesion in the occipital cortex auditory and vestibular auræ such as sound and dizziness point to the temporal lobe olfactory and gustatory auræ toward a site beneath the temporal lobe complicated mental states and dreams toward temporal and parietal lobes Somatic motor and sensory fits indicate the Rolandic cortex initial loss of consciousness with contralateral or upward turning of head and eyes the frontal pole a chain of autonomic phenomena the diencephalon etc

In general a fit which originates in the right hemisphere is apt to be associated with a turning movement of head and eyes to the left and vice versa But this contralateral turning not infrequently is followed quickly by the reverse turning movement so that it becomes necessary for the observer to see the very beginning of the attack Turning movements may be absent or in exceptional cases may be toward the side of the tumor

Seizures associated with tumors usually are recognized more easily as focal than are the seizures of an idiopathic epileptic but there is no other

two decades usually is to be placed in that vague group called idiopathic Commencing within the next two decades usually it is associated with cerebral tumor Thereafter renal and cerebral vascular diseases become increasingly frequent as the cause of convulsive seizures but the possibility of cerebral tumor should always be borne in mind even in patients in these later age periods

Neurological Examination

Careful neurological examination is of the greatest importance The advent of pneumography has in no way rendered this part of the patient s study less important Neurological examination frequently does not localize an expanding lesion with the certainty of ventriculography and yet neurological examination is the only means of estimating the extent and nature of interference with cerebral function

Any examination should include the head Local enlargement or tenderness sometimes may indicate the position of a tumor A large tumor invading the orbit from the anterior or middle fossa occasionally causes ipsilateral exophthalmos Enlarged veins and arteries in the scalp are of importance and auscultation of the cranium may indicate arterio venous connections In the general examination a search should be made for a possible primary focus for metastasis especially for pulmonary mammary renal and prostatic neoplasms

The neurological examination should be complete This is not the place to describe such a procedure but further reference is made to it under the heading of syndrome groups In general the most helpful parts of this examination are 1) ophthalmological examination of the optic discs 2) determination of visual acuity and careful visual field examination for hemianopsia and enlargement of the blind spot 3) study of cranial nerves for functional asymmetry and nystagmus 4) comparative strength on the two sides of face hand and foot movements 5) tabulation of the deep reflexes in search of asymmetry increase on one side usually indicating a focus in the opposite hemisphere 6) search for asymmetry in superficial reflexes 7) examination of sensation particularly of two point sensation in hands and recognition of objects by touch stereognosis 8) tests of coordination of upper and lower extremities 9) evidence of mental changes

In general certain of the most obvious of the defects of function produced by cerebral lesions in different areas are indicated schematically in Fig 7 This subject is again referred to under the section of this chapter on Syndromes Produced by Tumors

sensory defects abnormal reflexes hemianopsia anosmia aphasia or other evidences of deficiency often remain for minutes or hours following an attack. These functions should be tested at the earliest opportunity following an attack. It is frequently of value to produce and observe an attack by means of hydration or by hyperventilation. Our plan for producing an attack by hydration which is a modification of that of McQuarrie and Peeler[9] is as follows — To the adult patient 3 000 to 6 000 c c of water is given by mouth during each 24 hours and pitressin 0 5 c c is administered intramuscularly every two hours. The amounts of water and pitressin are smaller for children. The patient is weighed before the regime and fluid intake and output and body weight are charted thereafter every 6 hours. The regime is continued until the patient has had a seizure or until fairly marked symptoms of overdosage have appeared as manifested by abdominal cramps excessive vomiting headache syncope or falling blood pressure. Such symptoms usually do not appear until there has been a gain of 2 per cent or more of body weight. A seizure can be produced occasionally during the course of voluntary hyperventilation (Foerster). The patient breathes very deeply and very fast for ten minutes. The test should be continued at least until the onset of carpopedal spasm. Since the hydration procedure causes swelling of the brain and increase of intracranial pressure it should be used cautiously in suspected cases of brain tumor. It is definitely contraindicated in the presence of papilledema or other signs of increased intracranial pressure.

In the series of infratentorial tumor cases studied by Penfield and Tarlov there were no seizures of Jacksonian type. In 17 per cent of the cases however there were small seizures of some sort. So called cerebellar fits are characterized by spasmodic rigidity of the body with retraction of the neck[11]. Such attacks probably are produced within the brain stem itself rather than in the cerebellum. In a true midbrain fit there may occur dissociated movements of the eyes and sudden alterations of pupillary size.

For the most part however tumors within the posterior fossa produce attacks of a different type. There may be sudden loss of balance a dizziness that passes over. There may be transient weakness of arm and leg of both legs or of all extremities associated with a feeling of numbness. This suggests transient circulatory insufficiency in the cerebral peduncles or in the whole brain stem.

Convulsive seizures of any type beginning after the age of twenty should suggest the possibility of intracranial tumor. Omitting the convulsions which occur so frequently in childhood associated with any fever we may say generally that epilepsy *commencing* within the first

and might well lead to operation upon the wrong hemisphere unless ventriculography were carried out. Paralysis of one or even both sixth cranial nerves may be produced by increased intracranial pressure apparently due to the long exposed course of these nerves upon the floor of the skull. Thus internal strabismus may have no localizing value.

Long continued pressure may produce a variety of unexpected symptoms. Hypopituitarism may result from downward pressure of a ballooned third ventricle into the sella turcica with atrophy of hypothalamic structures. This may be evidenced by increase of weight, torpidity, sensitiveness to cold, low metabolic rate, menstrual difficulty, etc. On occasion anosmia may be produced by downward pressure upon the olfactory bulbs.

The accidental placement of hemorrhages or exudates in the retina may give rise to visual defects that are strikingly suggestive of true hemianopsia. Accurate ophthalmoscopic examination and determination of visual fields will prevent mistakes on this score.

Localization by Simple Roentgenography

A great deal is to be learned from simple roentgenograms of the skull as to the existence and position of slowly growing tumors of the brain. Rapidly developing neoplasms rarely leave their mark upon the bony structure of the cranium. Heuer and Dandy found that plain x-ray films yielded information of diagnostic or localizing value in 45 per cent of their cases of brain tumor. In a later review Dandy[9] reported that absolute evidence of tumor was supplied in 15 per cent of cases and supportive evidence in 35 per cent. Excellent recent studies of roentgenography in relation to brain tumor may be mentioned[108 to 109].

Generalized Changes — Increase of intracranial pressure, if of long duration, produces tell-tale changes in the skull. *Convolutional atrophy* of the skull may be produced by long continued pressure of the convolutions of the brain upon the inner surface of the skull (Fig 8). These digital impressions may be more marked in the vicinity of an infiltrating tumor, but otherwise they are not localizing. At times there may be localized thinning of the cranium without convolutional markings over an expanding lesion. Separation of the sutures in children and enlargement of the head likewise may indicate increase of pressure but not localization of a lesion. With generalized increase of intracranial pressure the clinoid processes gradually are thinned and may disappear as in Fig 8. Also the sella turcica may become enlarged due to hydrocephalic downward bulging of the third ventricle.

False Localizing Signs

False localizing signs may appear as a result of increased intracranial pressure or because of dislocation of the brain by a slowly growing tumor Such focal signs arise from disturbance of function in the brain far distant from the site of the tumor Ignorance of their mechanism may lead to

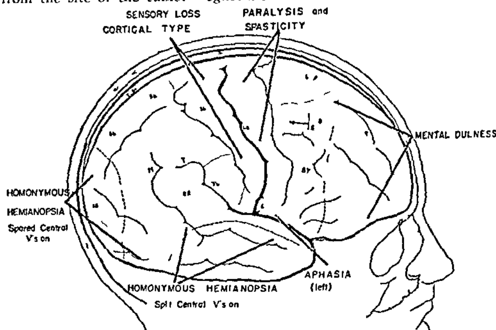


Fig 7 Localization of certain lesions in the cerebral hemispheres which produce obvious disturbance of function For details of motor and sensory function see figures 8 and 79

faulty localization Thus a neoplasm or subdural hematoma compressing one cerebral hemisphere may force the opposite cerebral peduncle against the sharp edge of the crus of the tentorium (as at B, Fig 4) The resulting evidence of a pyramidal lesion from the side opposite the tumor might lead to the mistaken conclusion that the tumor lay on that side In our experience this false localizing sign most often is due to a benign tumor or subdural hematoma which compresses the lateral aspect of one frontal lobe about half way between its anterior pole and the central fissure of Rolando

It is also possible for a large tumor compressing one hemisphere to displace the opposite posterior cerebral artery against the opposite crus of the diaphragm thus producing ischemia of the visual cortex on that side This results in homonymous hemianopsia on the same side as the tumor

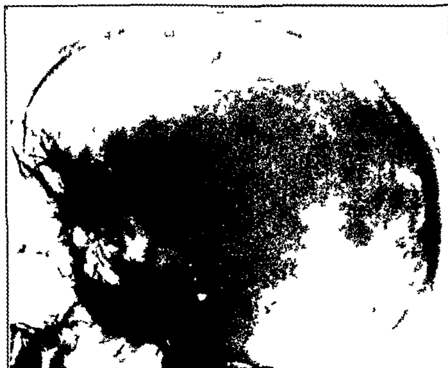


Fig 9 Case 63 Calcification in oligodendroglioma of frontal lobe Patient was 16 years of age

Type of Gliomatous Growth	*Number of Cases*	*Number showing Calcification*	*Per Cent*
Astrocytoma	[illegible]	6	21
Gliomatous cysts	31	0	0
Oligodendroglioma	1	1	100
Tuberosclerosis	3	0	0
Undifferentiated glioma	21	0	0
Astroblastoma	1	1	100
Spongioblastoma	30	6	20
Medulloblastoma	5	3	12
Total	131	17	13

Van Dessel[1b] studied 126 cases of verified cerebral gliomas from Cushing's material The tumor was demonstrated in roentgenograms in 17 instances (13 5 per cent) in 9 of which the tumor was located in the

Local Changes — Local roentgenographic changes due to tumor are uncommon but of obvious diagnostic and localizing value when present They may consist of calcification within the tumor itself or in abnormalities

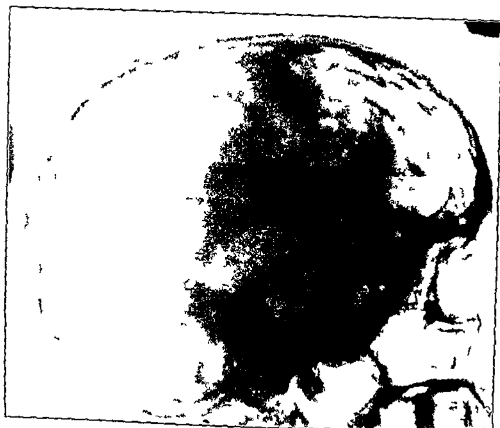


FIG 8 Case 1938 Convolutional atrophy of skull Patient age 25 had internal hydrocephalus due to obstruction of aqueduct of Sylvius The dilatation of the third ventricle had caused erosion of clinoid processes and enlargement of sella turcica

ties of the skull in the vicinity of the tumor The latter changes take the form of hypertrophy or erosion of bone localized convolutional impressions or alterations in the vascular channels of the skull

Heuer and Dandy[53] found that 6 per cent of their series of intracranial tumors showed some calcification Although calcification may occur in any type of tumor it is more common in the gliomas especially in the more slowly growing ones and is almost the rule in oligodendrogliomas (Fig 9) Masson[71] in reviewing 131 histologically verified gliomas listed the frequency of roentgenographically visible calcification as follows

and in the laminations surrounding old aneurysms and in these instances the shadow is likely to be rounded. It occurs occasionally in chronic subdural hematoma. Indeed it may occur in any neoplasm or parasitic cyst or following any localized destructive or inflammatory process within the brain.

It is essential to remember that calcification may occur normally in several intracranial structures. These include the choroid plexus (5.1 per cent of adults), the falx cerebri (7 per cent) and pineal body (51 per cent of adults). The falx and choroid plexus normally are not calcified in childhood, although the pineal is occasionally. Calcification in the choroid plexus usually is bilateral and occurs at the junction of the inferior ventricular horn with the ventricular body. Calcification in the falx commonly occurs in its anterior portion and takes the form of small bony plaques which usually are seen to lie upon one or the other surface of the structure.

Meningeal fibroblastoma (meningiomas) often give indication of their presence in roentgenograms. Sosman and Putman[111] studied 95 verified examples and found in the films recognizable changes characteristic of the tumor in 49 per cent.

These tumors frequently produce local bone changes. The fact that they are vascularized through the dura often results in enlargements of dural and scalp arteries and veins. The dural vessels may groove the under surface of the skull and the blood channels within the skull may dilate. This increased vascularity however may be either on the same or opposite side to the tumor, no doubt because attachment of meningeal fibroblastomas is so often at the vertex.

The behaviour of these neoplasms toward bone itself is unique, as described in the section on pathological anatomy. They may invade the overlying bone without eroding it. Growing through the Haversian canals the neoplastic cells produce new bone formation so that there may be internal and more often external thickening (Fig. 36). If the roentgenograms are taken so that the rays are tangential to the outer surface of the cranium, perpendicular rays of bone may be seen as in figure 11.

The majority of meningeal fibroblastomas do not infiltrate bone. They may produce a little thinning but thinning often is only apparent due to the fact that these tumors are apt to find origin in pacchionian granulations especially at the vertex. Large pacchionian granulations are apt to be found normally beneath vertical rarefactions of the bone.

In the anterior fossa meningeal fibroblastoma of the olfactory groove may cause alteration, usually thinning, of the cribiform plate or the crista

frontal lobe The degree of calcification may bear no relation to the size of the tumor It may spread evenly throughout the tumor or may be deposited in a single dense mass or be distributed in punctate fashion The shadow is often faint Stereoscopic plates are necessary to localize

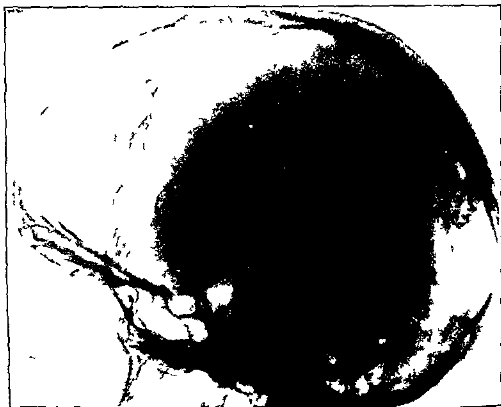


FIG 10 Case 3139 Calcification in epithelioma of hypophyseal duct above sella turcica Patient age 19

the position of the shadow accurately Linear streaked hair pin shadows are characteristic of oligodendrogliomas[6]

Calcification is common in hypophyseal duct epitheliomas whether they be cystic or solid (Fig 10) It frequently outlines a cyst wall in annular punctate fashion above the sella or extends into its base in the sella This type of shadow above the sella turcica in a young person and particularly if it outlines a cyst is pathognomonic of such a neoplasm

On the other hand hypophyseal adenomas rarely are calcified Calcification is not uncommon in tuberculomas in the walls of old abscesses

and in the laminations surrounding old aneurysms and in these instances the shadow is likely to be rounded It occurs occasionally in chronic subdural hematoma Indeed it may occur in any neoplasm or parasitic cyst or following any localized destructive or inflammatory process within the brain

It is essential to remember that calcification may occur normally in several intracranial structures These include the choroid plexus (5 1 per cent of adults) the falx cerebri (7 per cent) and pineal body (51 per cent of adults) The falx and choroid plexus normally are not calcified in childhood although the pineal is occasionally Calcification in the choroid plexus usually is bilateral and occurs at the junction of the inferior ventricular horn with the ventricular body Calcification in the falx commonly occurs in its anterior portion and takes the form of small bony plaques which usually are seen to be upon one or the other surface of the structure

Meningeal fibroblastomas meningiomas often give indication of their presence in roentgenogram Sosman and Putman[111] studied 95 verified examples and found in the films recognizable changes characteristic of the tumor in 49 per cent

These tumors frequently produce local bone changes The fact that they are vascularized through the dura often results in enlargements of dural and scalp arteries and veins The dural vessels may groove the under surface of the skull and the blood channels within the skull may dilate This increased vascularity however may be either on the same or opposite side to the tumor no doubt because attachment of meningeal fibroblastomas is so often at the vertex

The behaviour of these neoplasms toward bone itself is unique as described in the section on pathological anatomy They may invade the overlying bone without eroding it Growing through the Haversian canals the neoplastic cells produce new bone formation so that there may be internal and more often external thickening (Fig 36) If the roentgenograms are taken so that the rays are tangential to the outer surface of the cranium perpendicular rays of bone may be seen as in figure 11

The majority of meningeal fibroblastomas do not infiltrate bone They may produce a little thinning but thinning often is only apparent due to the fact that these tumors are apt to find origin in pacchionian granulations especially at the vertex Large pacchionian granulations are apt to be found normally beneath vertical rarefactions of the bone

In the anterior fossa meningeal fibroblastoma of the olfactory groove may cause alteration usually thinning of the cribiform plate or the crista

cally Less often there is thinning or hyperostosis of the roof of the orbit due to tumor beneath the frontal lobe Meningeal fibroblastomas of the lesser wing of the sphenoid may give rise to diverse but important localizing changes David and Stuhl[33] who made a roentgenographic study of

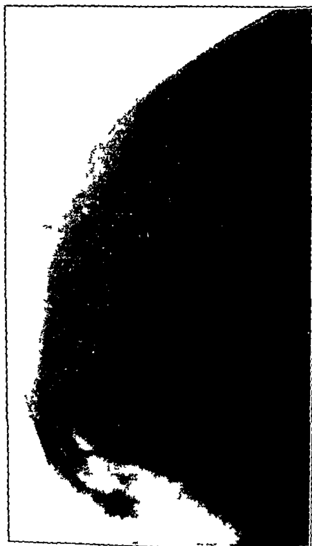


Fig 11 Meningeal fibroblastoma of frontal region that has grown through the frontal bone and caused new bone formation externally as shown by the palisade like streaks in the new formed bos Patient 18 years old (After Penfield 1923)

23 such verified cases found helpful diagnostic evidence in 8 instances Irregularity erosion or thickening of the sharp edge of the lesser wing

of the sphenoid may occur along with widening of vascular channels and occasionally unilateral alterations of the sella turcica or penetration into the orbit

Sarcoma in contradistinction to meningeal fibroblastoma of the dura erodes the overlying skull and may present a soft cone on the exterior Growths within the cerebral substance may produce moderate local erosion of bone or increased vascular markings especially if they are located near the surface Metastatic tumors of the skull are apt to pro duce punched out areas which may be mistaken for pacchionian impres sions in the bone

Hypophyseal tumors intrasellar produce characteristic lengthening enlargement and finally ballooning downward of the sella turcica into the underlying sphenoid sinus (Fig 12) The anterior clinoids become under cut and thinned sharpened and sometimes elevated while the posterior clinoids are apt to be pushed backward and absorbed The tumor may erode through the floor of the sella into the sphenoid sinus Tumors pressing down upon the sella from above craniopharyngiomas tumors of the third ventricle meningeal fibroblastomas of the sphenoid ridge seldom cause significant enlargement of the sella nor depression of its floor but they frequently produce some flattening and cause moderate atrophy or depression of the clinoid processes (Fig 10)

Tumors or aneurysms in the middle fossa are apt to cause absorption of the outlines of the sella as in Fig 22 In general the nearer the neoplasm is and the slower its growth the more destruction of the clinoid processes is produced Large tumors in the frontal lobe however are apt to cause absorption of the posterior rather than the anterior clinoids Tumors in the posterior fossa may cause antero posterior enlargement of the sella turcica due to absorption of the posterior clinoids and dorsum sellae This absorption no doubt is caused by the secondary internal hydrocephalus

Certain special exposures are necessary to demonstrate the early and important bony changes associated with tumors in certain locations Perineurial fibroblastomas of the eighth nerve usually develop within the internal acoustic meatus and cause enlargement of the meatus by early erosion of the bone There was little success in demonstrating this until Towne[119] suggested a posterior projection devised by Chamberlain in which the petrous bones are shown in profile and can be compared on one set of stereoscopic films The best way of comparing one internal auditory meatus with the other however is by stereoscopic views of the base of the skull which also demonstrate the size and shape of other foramina Special exposures are necessary also to demonstrate the optic

canal which may become widened or distorted by tumor of the optic nerve or other tumors invading the region from the anterior or middle fossa

Pineal Shift — Naffziger[84] was the first to draw attention to this valuable localizing method The pineal body is calcified and casts a shadow in 51 per cent of all cranial roentgenograms in adults[40] Naffzi



Fig 12 Case 1770 Eosinophilic adenoma of pituitary associated with acromegaly Patient age 44

ger[84] found that the pineal cast a shadow in 15 5 per cent of patients even under the age of 20 An expanding lesion on one side of the midline of the intracranial chamber often displaces the pineal shadow to the opposite side A shift of anything over 2 mm should be considered significant and displacement occurs up to 3 cm A tumor below the pineal may elevate the shadow and one above it may push the pineal downward Vastine and Kinney[11] have published graphs from which the normal position of the pineal shadow can be determined In lateral views it lies about 3 cm obliquely above and behind the apex of the petrous shadow Dyke

careful study[40] showed that shift of the pineal could be recognized in 56 per cent of patients with glioma and 44 per cent of patients with meningeal fibroblastoma

It should be remembered that atrophy of one hemisphere with or without meningeal cerebral cicatrix may cause a small amount of displacement of the pineal towards the involved side This possibility must be borne in mind always before concluding that the pineal is pushed away from an expanding lesion in the opposite hemisphere

Pineal displacement unlike other roentgenographic changes may be seen in rapidly growing tumors and it is particularly helpful in rapidly growing glioblastomas which are most frequent after middle age and which are apt to give no other roentgenographic change unless gas is injected

Ventriculography and Encephalography

Ventriculography the direct introduction of air into the ventricles through a trephine hole and encephalo raphy the introduction of air by lumbar puncture are procedures of the greatest value originally introduced by Dandy[5, 23] They have been much elaborated throughout the world[57, 58, 41]

Technique — In the case of brain tumor these procedures should be carried out only in a neurosurgical clinic or where a neurosurgeon is immediately available because after either procedure has been carried out operative removal of the neoplasm should be made the same day as a rule If operation is not immediate some of the gas may be removed but nevertheless its introduction into the ventricles is apt to result in a further increase in pressure during the ensuing two or three days resulting not infrequently in sudden death To lessen this reactive increase of pressure we have found it better to use oxygen than air It is absorbed more rapidly and actually may cause a marked fall in pressure for a time after its injection because of its ready absorbability

Encephalography usually is contra indicated if the pressure is raised and particularly if the lesion is suspected to be in the posterior fossa In any case if encephalography is carried out in a case of suspected tumor the injection should be made without morphia and usually should be limited to 40 or 50 c c of oxygen The spinal fluid pressure should be kept high all through the procedure even though more oxygen is injected than fluid removed If the intracranial pressure is normal and supratentorial neoplasm is suspected the patient should be seated (Fig 13) with the neck flexed so that the oxygen will pass up the aqueduct of

Sylvius without entering the basal cisternae and cranial subarachnoid spaces

In case a subtentorial tumor is suspected, and the intracranial pres



FIG 13 Encephalography Oxygen is drawn from sterile rubber bag into syringe through three way stopcock and is then injected in 5 or 10 c c amounts into spinal canal through lumbar puncture needle Spinal fluid is withdrawn and ejected by means of the stopcock and tubing into the glass tumbler At intervals the pressure is measured by the Ayer manometer which is inserted into the stopcock and may be laid aside when not in use To ensure the gas going only into the ventricles the head may be bowed till further forward

sure is not high the spaces in the posterior fossa may be demonstrated in the following manner the patient is placed in the prone position after the *lumbar puncture needle has been inserted satisfactorily* In this position and with the patient's face down and the head of the bed elevated 50 c c of oxygen replacing fluid will fill the fourth ventricle and *posterior cisterns* and the *patient may then be lifted without change of* position to the x ray table and lateral and postero anterior plates taken

Ventriculography is preceded by the making of trephine holes inspecting the pia and suturing the scalp It is our custom like that of Dandy to make two holes one over the occipital lobe of each side 5 cm above *and 5 cm lateral to the external occipital protrusion This position is* chosen because a careful visual field examination eliminates the possibility of tumor there and thus avoids the danger of puncturing a neoplasm A blunt brain needle then is passed into the ventricle and the head is tipped so that fluid will drain downward into the needle The *fluid is replaced by oxygen quickly from 10 to 30 c c being ample to* give good filling as a rule The ventricle opposite to the probable side of tumor is selected for puncture The holes may be made the day before *The puncture is done after plans have been made for immediate operation* should it be indicated

After the introduction of gas into the lateral ventricles by either method the most satisfactory routine is the following Place the patient on his back with brow up Take a true antero posterior view and a lateral view *without changing the position Then place the head in the three* other positions possible with the patient recumbent i e *with the* left side of the head up occiput up and right side up In turning the patient the aqueduct should be kept slanting upward so that gas cannot run outward toward the *fourth* ventricle and thus be lost in the subarachnoid spaces *On reaching* each position the head should be oscillated slowly so *that* the gas can find its way into the uppermost portions of the ventricular system Then leave the head quite still in each position while plates are taken With left side *up take a pair* of lateral stereoscopic films and the same with the right side With the occiput uppermost take a true postero anterior film and a pair of lateral stereoscopic films

Thus with the brow up the anterior parts of the ventricles are filled completely With each side up one *inferior* horn will be filled completely *and with the occiput up the* posterior ends of the lateral ventricles will be filled and the posterior end of the third ventricle aqueduct and fourth ventricle should be shown If there is particular interest in *the* fourth ventricle it is well to make the occiput up the first position No judgment should be made of the shape and position of any portion of the

ventricle unless it is in such a position as to be filled completely otherwise misinterpretation is frequent

Interpretation —The use of a rigid ventricular model such as that of Torkildsen made by the George P Pilling and Son Co Philadelphia Pa helps greatly both in interpretation and posturing the head for roentgenography We have found it simplest[118] to subdivide the lateral ventricle into six portions the extent of these portions as seen laterally are shown in D Fig 14 Each of these portions of the lateral ventricle casts a somewhat separate shadow when seen in antero posterior views as indicated by B and C in Fig 14 B shows what may be seen with brow up A–P view portion 1 being placed a little more lateral portion 2 more

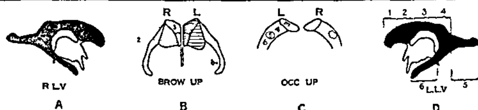


FIG 14 Normal ventricular outlines A right lateral ventricle and third ventricle B portions of ventricular system filled in brow up position C portions of system filled with occiput up (Posterior end of third ventricle aqueduct and fourth ventricle may be seen in this position but are omitted) D left lateral ventricle divided into the six arbitrary portions which are separable in B and C —see text

vertical and portion 3 more horizontal The anterior end of portion 6 or tip of inferior horn often is filled in this position and portion 4 may be depending on how much gas is present When the occiput is uppermost portions 3 4 and 5 are visualized

Typical alterations of the ventricular system produced by tumors in different localities are now given below using the diagram described by McConnell and Childe[78, 79] The legend explains each case and the position and size of tumor have been drawn by the surgeon after operation into the sketch of the cranial cavity (The surgeon in each case was either our associate Dr William Cone or one of us W P The ventricular outlines were kindly drawn in for us by our radiological associate Dr Arthur Childe) or in the case of the tumors of the brain stem by the roentgenologist after post mortem It might be well for the reader to study Fig 15 with the corresponding legend before proceeding

As explained in the previous section on Intracranial Alterations Produced by Expanding Lesions it will be noted that the ventricle on the side opposite to the tumor usually dilates (Figs 15 16 17 and 18) It

must also be borne in mind that when a portion of one lateral ventricle is pushed across into the opposite cranial chamber it must pass under the falx with its surrounding tissue It therefore drops down (Fig 16 brow up) to do so even when the tumor is placed near the base of the

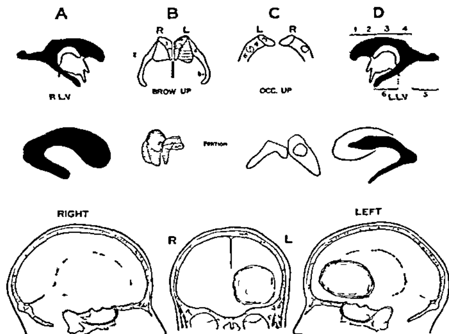


Fig 15 Large infiltrating tumor of left frontal lobe In brow up position the anterior ends of the ventricles are pushed from L to R across the midline which is indicated by the dotted line Portion 1 on left is lifted Portions 1 and 3 are dilated on the right and the third ventricle is collapsed In occiput up position there is also seen shift from left to right The lateral views show the right lateral ventricle (RLV) to be enlarged the left lateral ventricle (LLV) to be raised and pushed back anteriorly and the inferior horn (portion 6) to be thinned

skull as in Fig 17 In this figure the straight linear depression in LLV is the imprint of the falx and not the impression of the tumor The mechanism of this downward movement will be made more evident by reference to Fig 1 Those parts of the ventricles which do not contain choroid plexus may be obliterated easily by pressure e g portions 1 and 5 of the lateral ventricles But portion 6 which contains choroid plexus throughout may be displaced but rarely is obliterated

The septum pellucidum lies between portions 2 of the lateral ventricles as shown in A and B of Fig 18 It is normally directly above and in

line with the third ventricle when seen antero posteriorly It also lies more interior than the third ventricle so that an expanding lesion far forward in the frontal lobe displaces it to a greater distance across the midline than it does the third ventricle

Reference to Fig 18 indicates the cross section anatomy of the brain

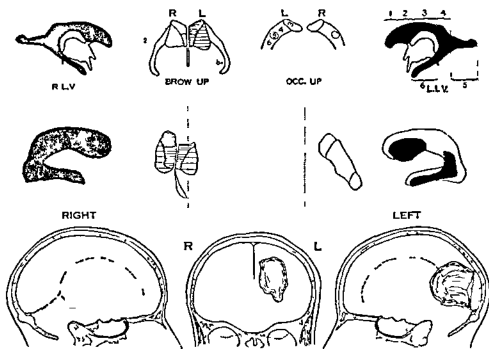


Fig 16 Left occipital tumor In brow up position the septum pellucidum (between portions 2) is seen to be displaced across the midline and portions 2 and 3 of left side are lowered as they pass under the falx from L to R Occiput up position shows left posterior end of ventricle to be obliterated In lateral views right lateral ventricle is enlarged Left lateral ventricle shows filling defect

as influenced by a neoplasm and this may be compared with the roentgenogram (Fig 19) which shows the actual displacements produced by such a tumor Figs 20 and 21 show normal ventricular shadows with no displacement of any sort (See also the excellent study of the normal encephalogram by Davidoff and Dyke[3]) It must be borne in mind that advancing years bring gradual enlargement of the ventricles even under normal conditions if senescence may be called normal Fig 22 shows the upward displacement of the inferior horn by a tumor of the temporal lobe as seen in the lateral view with the left side up

In demonstrating the aqueduct and fourth ventricle as in Figs 23 and 24 the oxygen should be introduced directly into the ventricles with

out allowing the intraventricular pressure to fall The head posturing must then be carried out with the patient lying prone as described above In Fig 23 the lesion evidently was small and in the vicinity of the pineal gland and operation therefore was carried out immediately In the

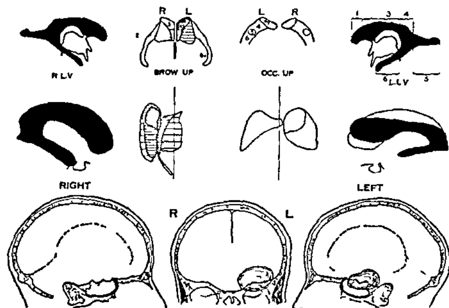


FIG 17 Tumor in left middle fossa has produced marked displacement of third ventricle and anterior portions of both lateral ventricles The left lateral ventricle (portions 3 and 4) is lowered not raised because it must pass under the falx to get to the other side of the skull The tip of the left inferior horn (portion 6) is obliterated

case of Fig 24 the lesion obviously was infiltrating the pons and consequently no operation was attempted but the post mortem photograph is shown in Fig 25

Other contrast media have been recommended for introduction into the ventricle Lipiodol ascendens is an opaque oil of less specific gravity than the heavier lipiodol ordinarily used to outline spinal lesions This lighter lipiodol which rises from the spinal canal and coats the walls of the ventricles is not to be recommended as it causes reactions and gives incomplete and misleading pictures

Thorotrast an opaque liquid discussed in the next section also has been used to outline the ventricles[49] but it is mentioned only to be condemned completely as it is rapidly irritating to ependyma and leptomeninges and may produce obstructive hydrocephalus[115]

Arteriography

This procedure has a very limited field of usefulness It was introduced by Moniz in 1927 and has been described repeatedly by him since that time[76] An opaque liquid is injected into the internal carotid artery and roentgenograms are taken rapidly during the few seconds required

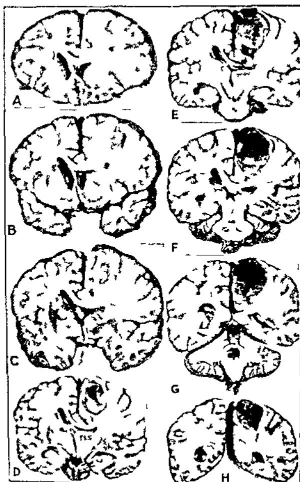


FIG 18 Frontal sections through the brain of patient with glioblastoma multiforme containing small cysts in left hemisphere A is the most anterior section and H the most posterior A and B show portion 2 of each lateral ventricle separated by septum pellucidum C D E and F show portion 3 of each ventricle that on the left being compressed and dislocated downward and toward opposite side that on the right being dilated Portion 4 of the lateral ventricles is shown in C and is dilated on each side The third ventricle appears only in C D and E and the aqueduct in F

for the pas a₆c of the liquid throu₆h the vascular tree A 25 per cent solution of sodium iodide was used first but because of unfavorable re actions this was repl iced by thorotrast thorium dioxide

The *technique* is as follows The patient is placed on the x ray table



Fig 19 Case 0,0 Ventricular displacement from left to right seen in brow up position Patient of 28 years had large hemangioendothelioma within the left frontal lobe Portion 1 seen faintly Left portion is lowered by the falx in its passage across the midline The third ventricle is tipped and displaced

and under local anesthesia the common carotid artery is exposed at its bifurcation by an oblique incision just below the jaw A warmed solution of thorium dioxide (from 8 to 12 c c) then is injected rapidly into the common carotid artery allowing the flow of blood to continue through the artery but occluding the external carotid branch Starting one second after the injection is begun two or three lateral roentgenograms are taken

is rapidly as possible by a pair of trained technicians The first roentgenogram shows the ipsilateral arterial tree (arteriogram) the second taken four seconds after the first shows the venous tree (phlebogram) The third may show thorotrast remaining in an area of slowed circulation

Interpretation — The blood which enters the posterior cerebral artery



Fig 20 Ventriculogram of normal individual in middle life brow up position Portions 1 2 and a small amount of the anterior end of 3 are shown also portion 6 of the right side in left side of picture The third ventricle shows in midline below septum pellucidum.

is derived normally from the vertebral arteries through the basilar artery Consequently only the middle and anterior cerebral arteries and their branches are commonly shown by the injection described above Characteristic displacements of these main trunks occur in the presence of space

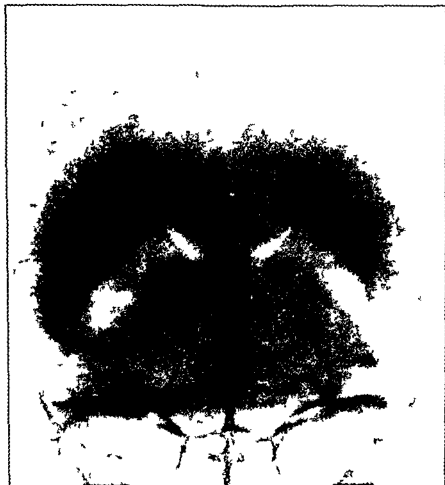


Fig 21 Ventriculogram normal same case as figure o occiput up position Portions 3 4 and 5 are visible also the posterior end of 6

occupying lesions and a hydrocephalus produces a larger curve in the course of the anterior cerebral artery[86 87]

Uses —Arteriography is unnecessary for the localization of brain tumors It is less exact than pneumography and helps only for certain

areas while ventriculography in experienced hands almost invariably gives the exact localization Furthermore arteriography brings a small risk of embolic and thrombotic accidents and a more serious objection is the possible threat of this substance to the patient in after years for thorotrast is a radioactive substance which is stored permanently in the reticulo endothelial system For summary of this aspect of the use of thorotrast see Reeves[103]

Nevertheless although arteriography has at present no place in the



FIG 22 Case 3581 Lateral ventriculogram left side up in case of meningeal fibroblastoma of the left temporal lobe Patient age 48 Note ventricular enlargement and elevation of inferior horn Erosion of clinoid processes has occurred

routine localization of brain tumors it serves a very useful purpose in localizing intracranial aneurysms arterio venous aneurysms and racemose hemangiomas A large arterio venous aneurysm or racemose aneurysm of one cerebral hemisphere instead of pushing the underlying ventricle away may cause enough local atrophy so that a ventriculogram suggests focal atrophy or scar rather than neoplasm An arteriogram under such circumstances establishes the diagnosis and indicates to the surgeon before operation the position of the strategically important arteries and veins In Fig 26 such an arterio venous aneurysm is demonstrated and in Fig 27 the lesion is shown at operation

Furthermore if ligation of one internal carotid artery for aneurysm

is considered the injection of thorotrast into the other internal carotid while the first artery is occluded by pressure gives insight into the advisability of the proposed ligation Differential diagnosis of glioblastoma multiforme has been undertaken by Tonnis who recognized a vascular pattern typical of this type of tumor

The decision of whether or not to use arteriography must be made

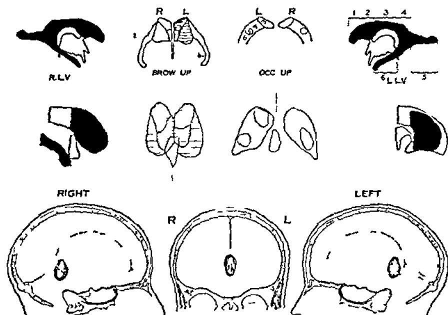


Fig 23 Ependymoma which produced dilatation of lateral and third ventricles Under LLV (left lateral view with occiput up) the aqueduct of Sylvius is seen to be pushed up and back by this small expanding lesion

after considering the gravity of the patient's outlook and after a thoughtful assessment of the differential diagnosis For example in the case of recurring subarachnoid hemorrhage from a congenital aneurysm the obvious dangers of conservatism must be weighed against the dangers of thorotrast and surgical ligation of the offending vessel

Syndromes Produced by Tumors Located in Various Parts of the Brain

There are certain sites of election for brain tumor within the cranial cavity The disturbance peculiar to the common sites may be outlined

briefly These syndromes are characteristic enough so that a shrewd localizing diagnosis often can be made on the basis of a discriminating history alone A tumor often compresses or invades parts of the brain contiguous to the area in which it grows so that the syndromes described are but patterns which delineate the basic disturbances due to tumors in

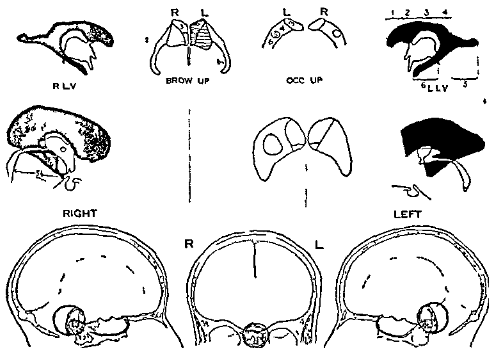


FIG 24 Tumor in floor of fourth ventricle Brow up position not taken The aqueduct and fourth ventricle are thinned out and displaced upward and backward The lateral ventricles are dilated The tumor which was cystic in its dorsal half is shown in figure 25

certain sites It is essential to remember that the one characteristic common to all intracranial tumors no matter what their location or type is advancing progression of the disturbance of neurological function The characteristics peculiar to the different tumor types are described further along in the section on Morbid Anatomy

Syndrome of the Cerebellopontile Angle

Tumors in this position usually prove to be perineurial fibroblastomas of the acoustic nerve less frequently meningeal fibroblastomas arising from the dura in this region or cystic collection of fluid due to arachnoiditis circumscripta

Perineurial fibroblastoma usually occurs in adult life. The majority of patients studied by Cushing [9] (this monograph will give valuable information) were between the ages of 20 and 50 when they came under observation and the average age was 38. The mild initial symptoms advance slowly and advice may not be sought until increased intracranial

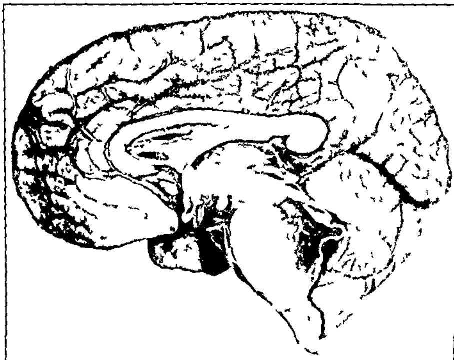


FIG 25 Brain from patient whose ventriculogram is recorded in figure 24. The cyst in dorsum of tumor is now collapsed. The ventriculogram showed clearly that the tumor was inoperable and no surgical procedure was attempted. Note that the cerebellum has been forced downward along the medulla oblongata to form a pressure cone

pressure is present. The history usually is of from one to six years duration and the sequence of events is of great importance. First there is disturbance of cochlear and vestibular function on the affected side with tinnitus and deafness. Dizziness may come in attacks or be fairly constant. Usually it is without a sense of rotation. So called cerebellar fits characterized by sudden weakness, numbness of the extremities, etc. are common and are described more fully under epileptiform seizures in the preceding section of this chapter and also under syndrome of the cerebellum further along.

briefly These syndromes are characteristic enough so that a shrewd localizing diagnosis often can be made on the basis of a discriminating history alone A tumor often compresses or invades parts of the brain contiguous to the area in which it grows so that the syndromes described are but patterns which delineate the basic disturbances due to tumors in

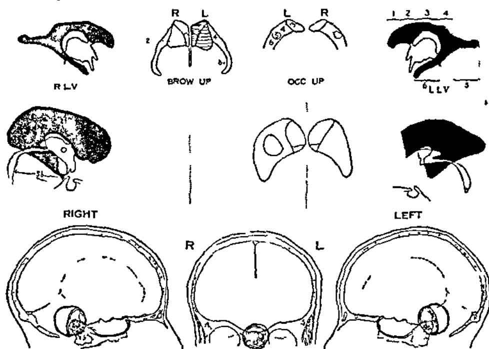


FIG 24 Tumor in floor of fourth ventricle Brow up position not taken Th aqueduct and fourth ventricle are thinned out and displaced upward and backward The lateral ventricles are dilated The tumor which was cystic in its dorsal half is shown in figure 25

certain sites It is essential to remember that the one characteristic common to all intracranial tumors no matter what their location or type is advancing progression of the disturbance of neurological function The characteristics peculiar to the different tumor types are described further along in the section on Morbid Anatomy

Syndrome of the Cerebellopontile Angle

Tumors in this position usually prove to be perineurial fibroblastomas of the acoustic nerve less frequently meningeal fibroblastomas arising from the dura in this region or cystic collection of fluid due to arachnoiditis circumscripta

Perineurial fibroblastoma usually occurs in adult life The majority of patients studied by Cushing [9] (this monograph will give valuable information) were between the ages of 20 and 50 when they came under observation and the average age was 38 The mild initial symptoms advance slowly and advice may not be sought until increased intracranial

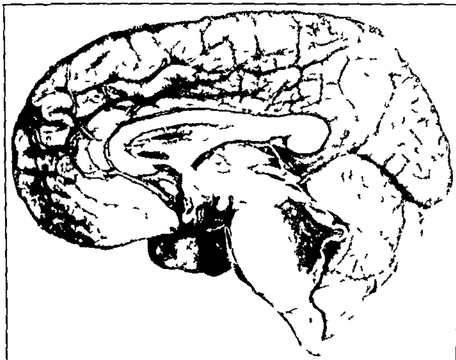


FIG 25 Brain from patient whose ventriculogram is recorded in figure 4 The cyst in dorsum of tumor is now collapsed The ventriculogram showed clearly that the tumor was inoperable and no surgical procedure was attempted Note that the cerebellum has been forced downward along the medulla oblongata to form a pressure cone

pressure is present The history usually is of from one to six years duration and the sequence of events is of great importance First there is disturbance of cochlear and vestibular function on the affected side with tinnitus and deafness Dizziness may come in attacks or be fairly constant Usually it is without a sense of rotation So called cerebellar fits characterized by sudden weakness numbness of the extremities etc are common and are described more fully under epileptiform seizures in the preceding section of this chapter and also under syndrome of the cerebellum further along

Enlargement of the tumor causes stretching or compression of those cranial nerves which are clustered in close proximity in the cerebello pontile angle producing the typical complaints of tinnitus deafness and dizziness as well as numbness of the face facial spasms difficulty in swallowing and articulation Ipsilateral cerebellar symptoms almost



Fig 26 Case 1088 Arteriogram (right side) of patient of 29 who complained of Jacksonian seizures and *increasing* paralysis of left arm Arteriovenous aneurysm (L) is shown in parietal region The right midd e cerebral artery (M) which enters it is en larged A anterior cerebral *artery* S carotid siphon as this part of the internal carotid is called by Moniz The arteriogram was carried out by our associate Dr Arthur El vidge Same case as figure 27

always are present and lead to clumsiness incoordination, staggering gait etc as described subsequently

Papilledema and headache as well as other signs of increased intra cranial pressure are apt to occur early among the disabling symptoms

which bring the patient to the physician A careful history usually in dicates however that mild local symptoms have long preceded the symptoms of increased pressure Although the course is in general progressive often there is a curious fluctuation of symptoms perhaps due to variations in the amount of encysted fluid surrounding the tumor

On examination the following are the most important signs diminution or loss of vestibular reactions and of hearing on the side of the tumor and ipsilateral loss of the corneal reflex or even more widespread trigeminal insensitivity There may be some stiffness or retraction of the



FIG 27 Operative photograph of the arteriovenous aneurysm which was demonstrated in figure 26 Arterial blood was flowing through these vessel directly into the longitudinal sinus above Block excision of the whole lesion including adjacent brain was carried out with excellent result

neck or the head may be held inclined towards the side of the tumor To these may be added ipsilateral weakness of the face involving fore head and eyelid as well as mouth lower motor neurone type of facial palsy Deviation of the pharynx in phonation to the opposite side indicates involvement of glossopharyngeal and perhaps vagus nerves deviation of the tongue to the ipsilateral side when protruded indicates involvement of the hypoglossal nerve on the same side and difficulty in swallowing suggests paralysis of the vagus

Involvement of the cerebellar nuclei on the same side is almost invariable as time passes This involvement is signalized by bilateral nystagmus which is coarser when the gaze is toward the side of the tumor In walking the patient deviates to the ipsilateral side and in standing with eyes closed he sways to that side There is also ipsilateral ataxia adiadochokinesia loss of capacity to check the moving limb and pass pointing to the ipsilateral side by the ipsilateral hand or foot Greater compression may give rise to contralateral pyramidal signs and sensory disturbances as well as to respiratory embarrassment as described in the earlier section on Intracranial Alterations Produced by Expanding Lesions Dislocation of the brain stem with compression of cranial nerves on the opposite side sometimes occurs and may prove misleading

Characteristic erosion of the porous acusticus often is visible in roentgenograms and may be of great diagnostic value especially in early cases (see in section on Localization by Simple Roentgenography)

Other tumors in the cerebello pontile angle cause similar symptoms and the type often is not disclosed until operation A sequence of symptoms which does not begin with cochlear or vestibular disturbance probably is not due to 8th nerve tumor and the presence of normal hearing and vestibular reactions is almost certain evidence against such a tumor Meningeal fibroblastomas have a steadier nonfluctuating course Circumscript arachnoiditis may be identical in symptomatology A variety of other lesions such as aneurysms parasitic cysts etc may or may not have special identifying characteristics Bilateral neurofibromas may occur on the 8th nerves as a part of von Recklinghausen s disease and Gardner and Frazier[5] have described such tumors even in the absence of other signs of neurofibromatosis

Syndrome of the Cerebellum

The cerebellum is the most common site of brain tumors in children Astrocytomas often cystic are about twice as frequent as the malignant medulloblastomas which occur only in the cerebellum and usually in the

first decade of life In the adult astrocytomas are also the commonest type of cerebellar tumor Hemangioblastomas either cystic or noncystic occur almost exclusively in the cerebellum and almost always in adult life Tuberculomas are not infrequent in this location

If the lateral cerebellar nuclei are involved there is of course evidence of ataxia and hypotonia in the ipsilateral limbs deviation to that side on walking and nystagmus as just described for the angle tumors The deep reflexes usually are less active throughout but especially on the side of the tumor and the knee jerks are apt to be pendular The pendular quality may be brought out when the patient is sitting with his legs swinging freely at the knee Tapping on the patellar tendon then will produce a pendular swing without the checking of movement by normal muscle tone The patient is apt to walk with a staggering gait and to fall to the affected side when he turns quickly or stands with feet together and eyes closed

A midline lesion produces truncal ataxia which is most evident on standing or walking There may be little or no incoordination in the upper limbs Hypotonia with resulting hyporeflexia and pendular jerks sometimes is unequal on the two sides of the body Nystagmus sometimes is absent Propulsion or more often retropulsion and ataxia of speech are common In children who suffer so frequently from midline cerebellar tumors unsteadiness in walking and evidence of increased intracranial pressure may be the only signs of the lesion

Epileptic seizures of the usual type do not occur as the result of tumors of the cerebellum (see epileptiform seizures in previous section) So called cerebellar fits characterized by opisthotonos are in reality brain stem seizures due to epileptogenic discharge in the vicinity of the midbrain Sudden attacks of weakness of numbness in the extremities of dizziness and of unsteadiness occur in many cases and apparently are due to sudden circulatory disturbances in the pons and medulla oblongata The patient may fall in such an attack but rarely loses consciousness Such attacks are signals that the pressure in the posterior fossa is reaching a dangerous level

Increased intracranial pressure occurs early especially with midline tumors and it may be difficult to establish localizing signs The danger of lumbar puncture has been discussed in previous sections of this chapter

Some idea of the type of tumor likely to be found may be gained from the patient s age but otherwise decision awaits surgical exposure of the growth Special mention should be made of the hemangioblastomas which often are associated with hemangioma of the retina skin and viscera a

relationship first pointed out by Lindau[70] The patient s skin and retina should therefore be examined minutely when cerebellar tumor is suspected

Note should be made also of generalized cisternal arachnoiditis which may give rise to a picture indistinguishable from that of cerebellar tumor the diagnosis being established only at operation The reader is referred to the paper of Horrax[63] for a further discussion of this subject

Syndrome of Pituitary and Suprasellar Tumors

Suprasellar tumors often occur in childhood pituitary tumors more often later in life The suprasellar neoplasm is apt to compress structures of the hypothalamus and optic chiasm first and hypophysis later while the intrasellar neoplasm compresses the hypophysis first and the chiasm and even hypothalamus later in case it ruptures through the dural diaphragm that roofs the sella As described previously in this chapter under Localization by Simple Roentgenography an intrasellar tumor produces marked enlargement of the sella turcica (Fig 12) whereas a suprasellar tumor is apt to cause downward flattening of the clinoid processes and often there is calcification within the tumor above the sella (Fig 10)

Pituitary Adenomas —The clinical distinction between the various types of pituitary adenoma is based on the kind of endocrine change exhibited by the patient The local signs and symptoms are common to all types of intrasellar growth

Headache occurs early and may long precede other symptoms It is often bitemporal due perhaps to stretching of the structures of the sella turcica The patient sometimes gives the history of sudden relief of headache following which there may be a period of weeks months or years before headache returns This relief appears to be associated with rupture of the tumor from the confines of the sella

Pressure of the tumor upwards upon the optic chiasm leads to bitemporal hemianopsia failing vision and primary optic atrophy The visual field defect usually appears in one eye first and involves the superior temporal quadrant later affecting the same quadrant c field of the opposite eye As pressure increases the lower temporal quadrants become involved and there is typical bitemporal hemianopsia with macular sparing which sometimes is recognized by the patient as tunnel vision If pressure is unrelieved the nasal fields become involved also and complete blindness may ensue Rarely homonymous hemianopsia may occur by extension of the tumor backwards to involve one optic tract

Impairment of visual fields occurs in advance of ophthalmoscopic

signs of primary optic atrophy *Generally however some degree of pallor is recognizable by the time the patient comes under observation* In neglected cases fully developed optic atrophy may occur with the characteristic picture of chalky white but well-defined discs in which the cribriform areas remain well preserved Atrophy indicates irrecoverable injury to visual fibers Therefore by comparison of the degree and extent of optic atrophy to the visual field defect a rough assessment can be made of the possible restitution of vision which operation may promise

A number of rare symptoms may occur late when the tumor has extended beyond the sella Papilledema and other signs of increased intracranial pressure may appear and the evidences of choked disc become superimposed upon the preexisting primary optic atrophy *If the tumor envelops the optic nerves and seals off their subarachnoid sheaths* papilledema may not occur even in the presence of increased intracranial pressure Epileptiform seizures especially of the uncinate type may signalize extension to the nearby gray matter and diabetes insipidus may indicate pressure upwards into the overlying brain Anosmia facial pain and even strabismus have been described due to involvement of adjacent cranial nerves Although some of the above phenomena may prove confusing the findings of bitemporal hemianopsia primary optic atrophy and roentgenographic alteration of the sella turcica usually simplifies the diagnosis

Chromophobe adenoma of the pituitary produces no internal secretion of its own *It is the commonest of the adenomas and usually occurs in adult life after body growth is complete* Because of the slow development and the relative mildness of both pressure and endocrine symptoms the diagnosis often is missed in the early stages Its presence is made known first by evidences of hypopituitarism due to compression of the pituitary gland by the tumor There are regressive sexual changes with obesity loss of libido and potentia and amenorrhea and in males the secondary sexual characteristics are apt to disappear the body assumes the female configuration and growth of beard is retarded The basal metabolic rate *blood pressure and body temperature usually are low and the patient often is hypersensitive to cold* Torpidity and somnolence are common and excessive appetite for sweets and increased sugar tolerance indicate disturbance of carbohydrate metabolism Rarely actual destruction of the pituitary gland may produce the picture of Simmonds disease characterized by extreme emaciation regressive sexual changes markedly lowered basal metabolism and premature senility

This tumor is sensitive to radiotherapy but is treated best by transfrontal hypophysectomy followed by deep roentgen therapy It is our custom to give three series of deep x ray treatments directed to the sella

turcica In each series as much roentgen therapy should be given as the skin will stand An interval of six weeks to two months should separate each series Glandular therapy often is of benefit to the privative symptoms

Chromophile adenoma of the pituitary produces an endocrine secretion of its own which causes overgrowth of bones and viscera If the trouble begins during childhood or adolescence there is overgrowth along normal channels and gigantism results Hypersecretion commencing after closure of the epiphyses produces acromegaly which is characterized by prognathism coarsening of the features enlargement of hands and feet and tufting of the terminal phalanges as seen by roentgenography The skin becomes thicker there is deepening of the voice and hair of masculine distribution may increase over the body Despite the powerful appearance of the patient muscular weakness often is a prominent symptom Impotence in the male and amenorrhœa in the female are the eventual rule The basal metabolism usually is increased especially in the earlier stages and tachycardia hyperidrosis and enlargement of the thyroid may occur There is often a change in temperament characterized by irritability wakefulness lack of concentration and indecisiveness Disturbance of carbohydrate metabolism is common and leads to hyperglycemia diminished sugar tolerance and glycosuria which may be relatively unresponsive to insulin Women may complain of enlargement of the breasts and profuse lactation

The above symptoms may progress steadily or may increase and decrease in waves Sometimes progression of the disease is arrested permanently many of the symptoms diminish or disappear and there is spontaneous cessation of the growth changes

In general the activity of neoplastic adenoma cells is not identical with the activity of the cells of the intact gland Tumors of the pituitary body are apt to produce a kaleidoscopic effect upon patients which may well be due to over secretion of certain cells followed by under secretion when neoplastic compression begins This probably explains the fugitive acromegaly transient diabetes mellitus and fleeting hyperthyroidism It explains the acromegalic giants who show late tendency to adiposo genital dystrophy

Treatment here is like that described for chromophobe adenoma It is often well to give roentgentherapy before considering operation As a rule operation is carried out only after the appearance of visual phenomena such as bitemporal hemianopsia for this means that the tumor has lifted the chiasm and can be reached more easily

Basophile adenoma is rare and produces a characteristic picture which

was described first by Cushing[3] These tumors are small and produce their typical effect by means of their internal secretion while local pressure symptoms seldom if ever occur Young adults usually are affected The patient is plethoric and rapidly gains fat about the trunk Wide purple striæ quite different from the pink white striæ distentiæ appear over the abdomen hips and thighs Hypertension and polycythemia are apt to be present and hypertrichosis producing bearded women Headache is common although the tumors seldom grow to large size Wide spread decalcification of the bones may occur with subsequent kyphosis or even pathological fractures Polydipsia polyuria hyperglycemia and decreased sugar tolerance are noted occasionally Amenorrhœa or impotence is common The course may develop very slowly or very rapidly measured in terms of years

Pituitary basophilism resembles hyperadrenalism and cases of tumor of the adrenal cortex have been reported which exhibit the same clinical picture as that described above Furthermore cases of basophile adenoma have been found without the appropriate clinical picture and in other instances the pituitary tumor has been associated with adenoma or hyperplasia of the adrenal cortex It seems probable that the picture is one of a polyglandular syndrome which frequently is initiated by basophilic adenoma This subject has been reviewed by Hardee[51]

Radiation of the pituitary and adrenals is at present the favored form of treatment Good results have been reported in some cases

Hypophyseal duct epitheliomas craniopharyngiomas Rathke pouch cysts constitute about 30 per cent of pituitary neoplasms and as explained in the following section usually arise above although sometimes within the sella turcica They often make their appearance early in life Nine of the fourteen patients studied by Frazier[48] were between the ages of 7 and 17 and in the remaining cases they occurred at ages up to 50 On the contrary about 80 per cent of pituitary adenomas make their appearance after the age of 20 The development of symptoms may occur rapidly or slowly over periods of months or years

Due to pressure upon the chiasm or optic tracts these tumors are apt first to produce visual disturbance although headache may precede this in children When the tumor presents anterior to the chiasm there is usually a bitemporal hemianopsia bitemporal quadrant defect or a temporal hemianopsia in one eye When the tumor presents posterior to the chiasm there may be an homonymous hemianopsia due to involvement of one optic tract or occasionally a binasal hemianopsia Blindness is frequent and the optic discs show evidence of primary optic atrophy

There is usually marked clinical evidence of hypopituitarism due to

compression of the pituitary gland Children and adolescents may be dwarfed in stature and exhibit lack of development of the sexual organs and secondary sexual characteristics Obesity adiposo genital dystrophy may or may not occur In the adult the picture is that already described under the section on chromophobe adenoma Beckmann and Kubie[10] who studied 21 cases found endocrine changes of the types described above in each of 10 patients under the age of 20 and in 8 out of 11 older patients These tumors because of their position sometimes produce marked mental symptoms which only disappear slowly after operation

Extension of the tumor upwards into the base of the brain may compromise the infundibulum and adjacent structures thus producing diabetes insipidus or disturbances of water balance When a tumor has grown to large size papilledema and other signs of increased intracranial pressure may appear especially in children and finally there may be evidence of involvement of the adjacent cerebral hemispheres

These tumors are quite slowly growing usually cystic and quite often calcified Treatment consists in partial removal by transfrontal operation beneath the frontal lobe they are not radio sensitive In some cases good temporary results are obtained by puncturing the cyst with a long needle through the frontal lobe The cyst will may be fixed by injection of Zenker s fluid to prevent the cells from reforming fluid Because of the hydrocephalus that develops when these tumors become large they may be removed partially by an approach through the lateral ventricle a procedure practised by Jefferson

Other Causes of the Suprasellar (Chiasmal) Syndrome — In addition to the hypophyseal duct epitheliomas a number of less common lesions in the vicinity of the chiasm are apt to give rise to the characteristic picture of primary optic atrophy and bitemporal hemianopsia with little or no alteration of the sella The reader is referred to the papers of Cushing[21] and Frazier[48] for a more complete discussion but brief mention of these conditions is made here A general idea of their probable incidence in a series including all intrasellar and suprasellar lesions is supplied below from the figures given by McLean[81] In that series pituitary adenoma constituted 40 per cent and hypophyseal duct epitheliomas 25 per cent

Suprasellar meningeal fibroblastoma (10 per cent) arises from the dura over the chiasmatic sulcus and tuberculum sellæ and thus elevates the chiasm It occurs in middle age and the symptoms are insidious in onset and slow in progression Treatment consists in surgical removal

Glioma of the chiasm (8 per cent) occurs largely in childhood The visual field defects although frequently bitemporal in character are apt to be bizarre and the hemianopsia seldom is strictly vertical Extension

along the optic nerves often leads to enlargement of the optic foramina as seen in suitably taken roentgenograms and the anterior portion of the sella turcica may be expanded forward in a pear shaped enlargement Headache makes its appearance late About one third of the cases are associated with evidences of generalized neurofibromatosis (von Recklinghausen s disease) The condition is not susceptible to surgical treatment

Arachnoiditis of the chiasmatic cistern (8 per cent) causes thickening of the leptomeninges and a circumscribed collection of fluid in the supra sellar region The etiology is uncertain The picture often is identical with that of suprasellar tumor and the cause may be recognized only by encephalogram or at operation The results of surgical opening of these arachnoidal cysts are surprisingly good

Aneurysm (3 per cent) of the circle of Willis or its immediate branches may occur at any age and if saccular and unruptured may give rise to the chiasmal syndrome The symptoms are apt to progress in steps rather than steadily as in the case of tumor When leakage of blood occurs into the cerebrospinal fluid the diagnosis is relatively simple Careful history *may reveal one or more previous episodes suggestive of leakage and char*acterized by sudden severe headache stiffness of the neck photophobia ocular palsies or disturbed sensation over the trigeminal field Roentgenograms occasionally demonstrate calcification in the wall of the aneurysm or some bony erosion in the vicinity of the sella If aneurysm is suspected usually it can be visualized if present by the intracarotid injection of thorotrast as described in a previous section

In addition to the above chordoma pituitary carcinoma and retro pharyngeal tumors occasionally are responsible for the syndrome

Syndrome of the Frontal Lobe (Premotor)

By the premotor portion of the frontal lobe we refer to all of the lobe which lies anterior to the precentral or pre Rolandic gyrus in man It includes cortical areas 6a beta 8 and 9 of Vogt (Fig 28) and the structures beneath these areas in the anterior fossa of the skull Tumors in this location produce varying symptoms depending on their proximity to the motor or Rolandic cortex When well forward in the lobe motor signs and symptoms may be lacking or of late appearance The picture is then apt to be one of gradual mental and behavioural deterioration

There appear decrease in initiative concentration and memory in dolence untidiness faulty judgment childishness silly jocularity a lowering of moral or ethical standards and even somnolence or coma may occur as the lesion increases in extent Such symptoms are more pronounced

when the dominant hemisphere is involved left hemisphere in the right handed patients and especially when both frontal poles are invaded Involvement of the genu of the corpus callosum is said to produce apraxia or profound mental change although this picture we think is due to in

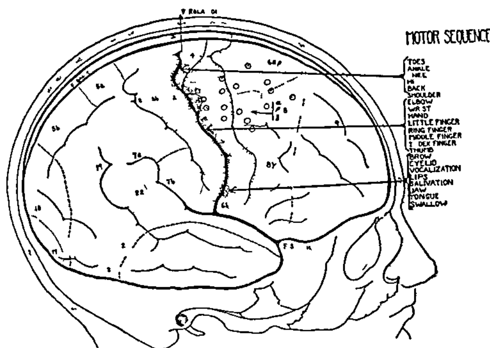


FIG 28 Diagram of somatic motor responses from stimulation of the human brain Each dot indicates a response The sequence as given in the column at the right is practically invariable but the exact location up and down the fissure of Rolando varies from case to case The circles indicate conjugate movements of the eyes (After Penfield and Boldrey 1937)

volvement of both frontal lobes rather than to interference with the function of the corpus callosum

It must be admitted that tumors of the frontal lobe sometimes give rise to no detectable sign and the decrease in planned initiative which probably is present may be attributed falsely to other causes Furthermore it should be remembered that mental symptoms resembling those due to frontal lobe tumor may result from cerebral arteriosclerosis or other organic diseases of the brain

Tumors in locations other than the frontal lobe may cause somewhat similar mental changes and this is particularly true of temporal lobe tumors Strauss and Keschner[114] who reviewed 85 cases of frontal lobe tumor with special attention to mental changes found abnormal mental

reactions at some time during the course of the disease in 90 per cent of patients In a similar study of 11_ patients with temporal lobe tumors Keschner Bender and Strauss[67] found abnormal mental reactions in 94 per cent They were unable to distinguish any significant difference in the type of mental abnormality observed in frontal and temporal lobe cases

Aphasia — When the dominant hemisphere is involved some degree of aphasia is noted in about half the cases In the absence of a visual field defect motor aphasia suggests a lesion in the frontal lobe of the dominant hemisphere The defect largely involves exteriorization of speech and may be so slight as to suggest mere slowness and mental retardation Because of the obvious lateralizing importance of aphasia the physician should school himself to recognize its mildest forms Confronting the patient with common objects is useless in cases of mild aphasia The patient must be asked to name more complex and uncommon objects such as may be pointed out in a picture book or the advertisements in a periodical Such tests within the obvious limits of the patient s education and mental caliber may reveal an unsuspected aphasic defect The aphasic patient is clever at concealing his deficiency but slight hesitancy in speech the use of an unusual word or one a little off the intended shade of meaning circumlocution the remark it s just slipped my mind for a moment or a slight misunderstanding of the examiner s questions may all point to the defect It is obvious that when aphasia is suspected all expressive and receptive functions should be tested carefully i e reading writing naming objects recognition of form etc

Due to involvement of fronto cerebellar pathways cerebellar signs may be prominent and may lead to false localization These signs usually appear in the extremities contralateral to the involved lobe and consequently a tumor of the right frontal lobe may lead to a mistaken left cerebellar localization and vice versa Thus coarse tremor nystagmus hypotonia pastpointing defects of posture and muscular incoordination may occur

Hyland and Botterell[68] found signs suggestive of cerebellar involvement in 6 out of 30 patients with tumors involving one or both frontal lobes The signs probably are produced by interference with the fronto ponto cerebellar pathways in the frontal lobe The occasional rapid disappearance of these signs after operation suggests that increased local pressure is an important factor

As Walshe and Robertson[13] and others have pointed out groping and grasping tonic innervation may be present in the contralateral hand or even in the foot The phenomenon is composed of two elements either one or both of which may be present — first a tendency for the limb to

when the dominant hemisphere is involved left hemisphere in the right handed patients and especially when both frontal poles are invaded Involvement of the genu of the corpus callosum is said to produce apraxia or profound mental change although this picture we think is due to in

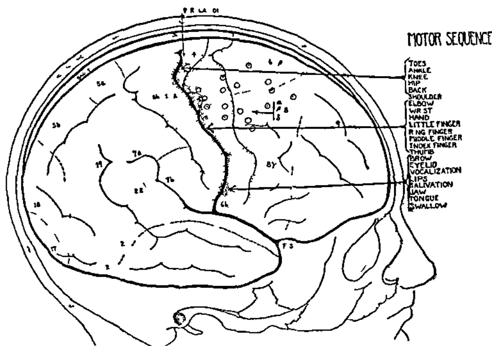


FIG 28 Diagram of somatic motor responses from stimulation of the human brain Each dot indicates a response The sequence as given in the column at the right is practically invariable but the exact location up and down the fissure of Rolando varies from case to case The circles indicate conjugate movements of the eyes (After Penfield and Boldrey 1937)

volvement of both frontal lobes rather than to interference with the function of the corpus callosum

It must be admitted that tumors of the frontal lobe sometimes give rise to no detectable sign and the decrease in planned initiative which probably is present may be attributed falsely to other causes Furthermore it should be remembered that mental symptoms resembling those due to frontal lobe tumor may result from cerebral arteriosclerosis or other organic diseases of the brain

Tumors in locations other than the frontal lobe may cause somewhat similar mental changes and this is particularly true of temporal lobe tumors Strauss and Keschner[114] who reviewed 85 cases of frontal lobe tumor with special attention to mental changes found abnormal mental

momentary lapse of consciousness without falling We have seen priapism in an attack when the neoplasm lay deep in the frontal lobe

A seizure arising in the frontal pole of the dominant hemisphere left hemisphere of a right handed man often is followed by transient aphasia

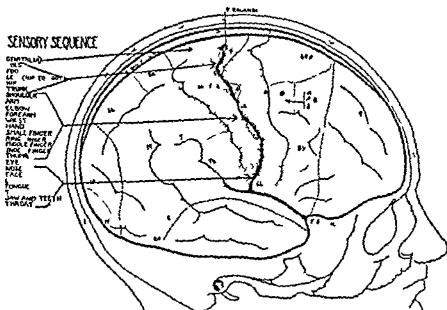


FIG 29 Diagram of sensory somatic sequence as in figure 28 The sequence is invariable although responses are at times obtained from the precentral gyrus The circles indicate sensation of movement of the eyes The type of sensation after electrical stimulation in order of frequency is tingling numbness sense of movement etc

in the recovery period The patient thus may regain consciousness before he recovers the capacity of speaking or using words properly

In cases of meningeal fibroblastoma mental disturbance cerebellar symptoms and epileptiform seizures are more likely to occur when the tumor grows from the vault parasagittal than from the base of the skull

Syndrome of the Rolandic Region

By Rolandic region we refer roughly to the precentral and postcentral gyrus and the immediately underlying tissue areas 6a alpha 6b 4 3 1 and 2 of Vogt (see Figs 28 and 29)

The area anterior to the Rolandic fissure mainly controls fine movements of the somatic musculature The area posterior to the fissure for

reach out and grasp an object brought into the patient's field of vision second a firm grasp made upon any object which is placed in the hand and which stimulates the skin or stretches the flexors of the fingers This is without the partly conscious element of groping and may occur in the comatose patient The grasp is maintained until the stimulation of stretch is removed The phenomenon is due most frequently to lesions near the midline in the frontal region but it is our observation that it may also result from large lesions placed elsewhere in the hemisphere Bilateral grasp reflex is of no localizing significance

A tumor in or near the under surface of one frontal lobe may by compression of the olfactory nerve cause diminution or abolition of the sense of smell on that side Elsberg[43] claims that by means of more elaborate olfactory tests he can obtain evidence of wide localizing value

By compression of the optic nerve the tumor may give rise to primary optic atrophy on that side and by obliteration of the subarachnoid sheath about the nerve prevent the formation of papilledema if increased intracranial pressure is present Papilledema eventually occurs in the other eye however and this dissociation Foster Kennedy syndrome first described by Gowers is of considerable localizing value as referred to under papilledema

Disturbance of bladder function characterized by urgency or incontinence are not infrequent and probably is due to interference with cortical mechanisms subserving vesical control Such symptoms were present in 25 out of 105 cases reported by Frazier[43] These patients often show a surprising lack of embarrassment when they have been incontinent

Even when one is alert to all of these possible sequels to destruction it must be remembered that the frontal lobe especially the non dominant frontal lobe is the largest so called silent area of the brain and large lesions often pass unsuspected for a considerable period On the other hand tumors here often produce recurring epileptiform seizures about 40 per cent of cases the pattern of which indicates the irritative focus

Epileptic discharge in the frontal pole is characterized by initial loss of consciousness followed presently by turning of head and eyes to the contralateral side and turning of the whole body in that direction (Fig 6) Instead of turning of eyes and head to the contralateral side there may be deviation of gaze upward or upward and somewhat across to the opposite side This initial loss of consciousness and the head turning usually are followed by convulsive movements in the contralateral extremities with raising of the contralateral arm and rapid generalization of the movements to involve extremities of both sides Small attacks from this region are apt to resemble classical petit mal seizures characterized by a

may be considerable ataxia in the hand or foot during finger nose or heel knee tests especially when the eyes are closed sensory ataxia

Jacksonian Seizures — It is from the precentral gyrus that classical Jacksonian seizures arise beginning in contralateral foot digit arm face or tongue etc and spreading through other portions of the body according to the order of representation indicated in Fig 28 before becoming generalized and involving all the extremities The same form of detailed Jacksonian march may be entirely sensory Thus a focal point in the postcentral gyrus originates the discharge and a sensation of tingling or numbness in one contralateral part spreads through other contralateral parts according to the representation indicated in Fig 29 The whole fit may be characterized by sensory phenomena only or there may be a spread to motor convulsive movement in which case the motor movements are apt to begin in the same part which first experienced the sensation

It should be pointed out also that vocalization is represented in the *precentral gyrus of each hemisphere as indicated in Fig 28* The epileptic cry may therefore be an evidence of cortical discharge without reference to the so called speech area

In general an epileptic discharge never begins in a tumor It begins in the cerebral grey matter adjacent to that tumor Thus a lesion lying anterior to the precentral gyrus may influence area 6a alpha sufficiently to produce increased tone in one or both contralateral extremities without paralysis for spasticity in the contralateral limb is produced by disturbance of function in area 6a alpha It may then give rise to seizures originating in the adjacent motor area characterized by a Jacksonian march Likewise a lesion posterior to the postcentral gyrus may give rise to a seizure characterized by a sensory march Furthermore motor and sensory gyri are so bound together by connecting neurones that stimulation anterior to the central fissure occasionally gives rise to sensation alone and vice versa as indicated by the dots in Figs 28 and 29

An epileptic discharge beginning in the general vicinity of the Rolandic cortex of the dominant hemisphere does not produce speech but may be *followed by aphasia just as transient paralysis in the postconvulsive period* often involves the extremity that has begun an epileptic dance

Deviation of the eyes to the contralateral side associated with opening of the eyelids may be produced from the general vicinity of area 8 see small circles in Fig 28 and this may be the initial feature of a Jacksonian march Area 6a beta Fig 28 has been called the frontal adversive field *to indicate that adversive movements to the opposite side may be produced* by stimulation here But this is a little misleading It is true that

the most part subserves discriminative sensation Tumors in this region give rise to contralateral motor paralysis to sensory loss of cortical type or to a combination of the two and these symptoms appear quite early i e when the lesion is still quite small

If the lesion is placed in the anterior lip of the central fissure in area 4 it may give rise to flaccid paralysis of one contralateral extremity (Fig 28) If it involves the whole precentral gyrus or the anterior portion of it i e area 6a alpha alone it gives rise to a spastic paralysis of the contralateral limb The awkwardness spasticity or muscular weakness is of course greatest in that part of the body represented by the cortical area in which the tumor lies The face and hand are involved first more often than the foot because of their larger representation in the cortex Motor paralysis in the limbs is characterized first by loss of small movements of hand or foot followed in turn by loss of the larger and less complicated movements Though these defects may be exquisitely localized to a single part of the body at the beginning they spread during weeks or months eventually producing a spastic hemiplegia

Neoplasms in or near the Rolandic region even when they produce no obvious motor or sensory defect are apt to alter the reflexes on the opposite side of the body These alterations include loss of the abdominal and cremasteric reflexes and the presence of Babinski s sign as well as increase in the deep reflexes of the arm or the leg depending upon which representation is nearer the tumor

If a neoplasm lies posterior to the central fissure the defect is apt to be predominantly sensory It involves foot when placed high near the longitudinal fissure hand if near the middle and face if low according to the sequence of representation indicated in Fig 29

There is usually a moderate sense of numbness in the affected part and the patient may complain that it feels dead or awkward Crude recognition of touch pain and temperature usually is somewhat reduced but is not otherwise affected The chief defect involves discriminative sensation The patient may be unable to distinguish degrees of intensity of tactile or painful stimuli and may be unable to point accurately to the site of stimulation He may be unable to distinguish the texture size weight or shape of objects placed in the affected hand Moderate degrees of heat and cold are not differentiated the shape of a large figure written on the skin is unrecognized and the patient cannot distinguish between one and two points of a caliper placed on the area Knowledge of the position of a limb in space may be faulty and this may lead to wandering movements static ataxia of the part which are sometimes sufficiently pronounced to suggest an extrapyramidal lesion In like manner there

whereas a lesion of the optic tract or of the temporal lobe results in a hemianopsia without such sparing. In 10 cases with occipital lobe tumor and hemianopsia studied by Horrax and Putnam[6] macular sparing occurred in 14 instances. A lesion above the calcarine fissure produces a quadrantic visual defect in the lower homonymous field and a lesion below the calcarine fissure produces an upper quadrantic defect. For discussions of the much vexed question of representation of central vision the reader is referred to Holmes and Lister[6], Holmes[61], Brouwer[13], Horrax and Putnam[6], Penfield, Evans and MacMillan[101]. Upper quadrantic

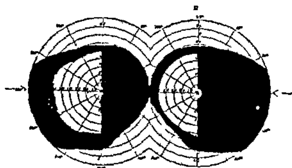


FIG 30. Case L. K. Right homonymous hemianopsia with sparing of central vision in the blind field produced by amputation of the left occipital lobe. (After Penfield, Evans and MacMillan, 1935.)

defects, however, are rare, whereas they are common in temporal lobe lesions.

Invasion of the region of the angular gyrus in the dominant hemisphere leads to defects of visual recognition (visual agnosia). The patient may be unable to read (alexia), to recognize the faces of his friends or to copy simple written figures or designs. He may not recognize an object which he sees, though he does so readily when it is placed in his hand. Some degree of auditory and verbal aphasia usually is present also.

Epileptiform seizures arising in the occipital lobe (Fig 6) usually are ushered in by a visual hallucination which may be seen in the homonymous contralateral field or straight ahead. If the discharge originates near the calcarine cortex, the visual phenomenon is a gross one, such as a light, often colored, or a scotoma. If the origin be more anterior and on the external aspect of the hemisphere, there may be sparkling lights or elaborate visual hallucinations such as a hooded figure, vivid scenes, people in motion, etc.

A large tumor in the occipital lobe may press upon the tentorium

discharge in this area occasionally may produce turning movements but not more often than in certain other portions of the frontal lobe[93]

Jacksonian attacks may long precede any other signs or symptoms of tumor The transient focal defects which follow attacks last longer as time goes on and finally tend to become permanent

Special mention should be made of the parasagittal meningeal fibroblastomas which straddle the longitudinal sinus and therefore may involve the foot area of the Rolandic cortex bilaterally Paralysis sensory loss reflex changes and Jacksonian attacks begin in one leg and later spread to the opposite leg An excellent discussion of these tumors will be found in Olivecrona s monograph[87]

Syndrome of the Parietal Lobe (Postsensory)

We would like to refer here to that portion of the hemisphere posterior to the Rolandic sensory cortex above the temporal lobe and anterior to the occipital lobe Lesions here often give rise to astereognosis in the contralateral hand and to other defects of discriminative sensation as described previously in the syndrome of the Rolandic region

Deep subcortical tumors may involve the optic radiation and give rise to homonymous hemianopsia in the contralateral visual field As the tumor grows downward it tends first to involve the uppermost fibers and thus to produce a lower quadrantic field defect in contradistinction to temporal lobe tumors which are apt first to involve the upper quadrants Small objects (1/2 000 2/2 000) should be used in conjunction with the Bjerrum screen to reveal early field defects In rare instances there may be merely a lack of appreciation of color or form Riddoch[104] has described visual agnosia in the contralateral visual field due to lesions in this area

Epileptiform seizures arising here occasionally begin with a sense of rolling over or falling out of bed but more often with sensory phenomena referable to the adjacent sensory cortex

Syndrome of the Occipital Lobe

Neoplasms confined to this lobe are uncommon Only 40 out of 1 881 verified intracranial tumors reported by Horrax and Putnam[65] were found in this location They usually give rise to homonymous hemianopsia either complete or partial If the visual fields are taken carefully it will be found that the homonymous defect does not include central vision That is to say there is sparing of central vision in the blind field (Fig 30)

Epileptiform seizures arising here (Fig 6) are ushered in most often by a buzzing or roaring sound usually referred to the contralateral ear and by dizziness If the lesion involves the under surface of the lobe there may be an hallucination of taste or smell nearly always with a disagreeable quality and often accompanied by involuntary licking or tasting movements or smacking of the lip uncinate fit Rarely sensations of thirst or of hunger may usher in attacks and in several of our cases the aura has consisted of musical sound

More complicated hallucinations may occur during a temporal lobe seizure when the discharge occurs more posteriorly Such hallucinations are micropsia of objects appearing small or distant and macropsia when objects become large or near Complicated dream states are experienced when a whole scene may be visualized or voices heard There often comes over a patient during or preceding a temporal lobe fit an overwhelming feeling of familiarity as though he had experienced the same thing somewhere before

Syndrome of the Diencephalon

The diencephalon includes the thalamus and in general the structures about the third ventricle Tumors here are apt to extend outward into the basal ganglia producing contralateral rigidity and a Parkinsonian attitude from involvement of structures not strictly included in the diencephalon

There may appear a pathological tendency to somnolence when the lesion is in the vicinity of the head of the caudate and anterior thalamus (Fig 32) If infiltration is wide the patient sinks into a continuing stupor Loss of pain sense or at times diffuse burning contralateral pain of the so called thalamic type occurs with involvement of the thalamus There may be unilateral disturbance of sweating throughout the body or other autonomic functions may be interfered with Diabetes insipidus characterized by polydipsia and polyuria is produced by tumors involving the tuber cinereum either directly or by pressure

Epileptiform seizures arising in the diencephalon may be characterized wholly or in part by autonomic phenomena such as flushing of face and neck sweating rise in blood pressure alteration of pulse rate etc (Penfield[19]) Such seizures may begin by autonomic phenomena and may spread to include somatic phenomena such as movement and sensation in the extremities Tumors of the third ventricle may give rise to autonomic epileptic seizures as in the case shown in Fig 33

Dandy[20] has reported a series of 21 apparently benign removable

and give rise to homolateral cerebellar signs but the visual field defect usually would place the lesion above the tentorium In the absence of macular sparing cerebral pneumography is sometimes the only means of distinguishing an occipital lobe tumor from one in the temporal or parietal lobe

Syndrome of the Temporal Lobe

Lesions here often give rise to homonymous hemianopsia which frequently is quadrantic and which as mentioned before does not spare

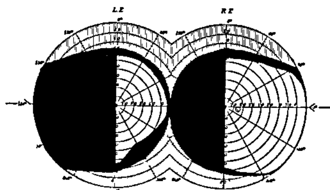


Fig 31 Case R M Complete left homonymous hemianopsia with splitting of central vision produced by a large lesion confined to the right temporal lobe

central vision (Fig 31) but cuts the field by a straight line The defect may be small and may appear as mere notching of the normal field of vision In the dominant hemisphere there is apt to be some degree of aphasia especially if the tumor involves the underlying island of Reil Exteriorized speech usually is most affected but there may be difficulty in understanding the spoken or written word Rather complicated mental disturbances not infrequently are encountered in tumors of the temporal lobe

A neoplasm lying on the under surface of the lobe occasionally compresses the third nerve and causes dilatation of the pupil and strabismus in the homolateral eye Loss of the corneal reflex or sensory defect on the face may indicate compression of the fifth nerve Bilateral or contralateral deafness diminished auditory acuity and altered vestibular responses have been reported but we have not been impressed with their significance Northington[82] studied 52 cases of intracranial tumor and found no specific auditory defects except when the eighth nerve was involved by subtentorial tumor McNally Erickson Scott Moncrieff and Reeves[83] have confirmed these findings

Epileptiform seizures arising here (Fig 6) are ushered in most often by a buzzing or roaring sound usually referred to the contralateral ear and by dizziness If the lesion involves the under surface of the lobe there may be an hallucination of taste or smell nearly always with a disagreeable quality and often accompanied by involuntary licking or tasting movements or smacking of the lips uncinate fit Rarely sensations of thirst or of hunger may usher in attacks and in several of our cases the aura has consisted of musical sounds

More complicated hallucinations may occur during a temporal lobe seizure *when the discharge occurs more posteriorly Such hallucinations* are micropsia of objects appearing small or distant and macropsia when objects become large or near Complicated dream states are experienced when a whole scene may be visualized or voices heard There often comes over a patient during or preceding a temporal lobe fit an overwhelming feeling of familiarity as though he had experienced the same thing somewhere before

Syndrome of the Diencephalon

The diencephalon includes the thalamus and in general the structures about the third ventricle Tumors here are apt to extend outward into the basal ganglia producing contralateral rigidity and a Parkinsonian attitude from involvement of structures not strictly included in the diencephalon

There may appear a pathological tendency to somnolence when the lesion is in the vicinity of the head of the caudate and anterior thalamus (Fig 32) If infiltration is wide the patient sinks into a continuing stupor Loss of pain sense or at times diffuse burning contralateral pain of the so called thalamic type occurs with involvement of the thalamus There may be unilateral disturbance of sweating throughout the body or other autonomic functions may be interfered with Diabetes insipidus characterized by polydipsia and polyuria is produced by tumors involving the tuber cinereum either directly or by pressure

Epileptiform seizures arising in the diencephalon may be characterized wholly or in part by autonomic phenomena such as flushing of face and neck sweating rise in blood pressure alteration of pulse rate etc (Penfield[29]) Such seizures may begin by autonomic phenomena and may spread to include somatic phenomena such as movement and sensation in the extremities Tumors of the third ventricle may give rise to autonomic epileptic seizures as in the case shown in Fig 33

Dandy[30] has reported a series of 21 apparently benign removable

tumors of the third ventricle which tended to give rise to intermittent headache dizziness and motor or sensory changes Internal and external ophthalmoplegias were common Ventriculography was of considerable aid in diagnosis

Syndrome of the Mesencephalon

Lesions involving the roof of the midbrain are apt to disturb the upper motor neurone centers which control conjugate movement of the eyeballs

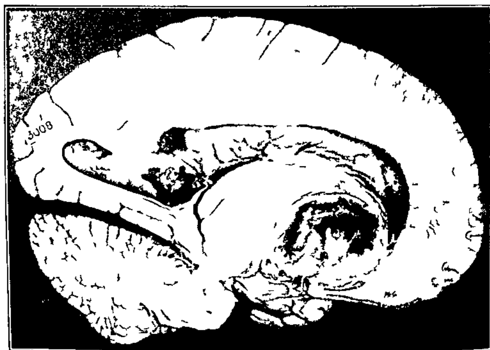


Fig 32 Glioma deep in anterior portion of the thalamus which produced (for 18 months before the patient s death) an unconquerable tendency to fall asleep The brain was cut in sagittal plane lateral to midline (Case 3008 used by permission of Dr Cone)

Deficiency of upward gaze is often the earliest symptom and this may be associated with retraction of the upper lids Voluntary conjugate deviation may be lost while reflex deviation is retained as evidenced by ability of the eyes to fix an object when the head is moved by the examiner There may be complete absence of conjugate movement and spasm or paralysis of convergence dilated and immobile pupils or asymmetrical nuclear ophthalmoplegias may occur Due to compression of important tracts there is often a variety of cerebellar sensory pyramidal extra

pyramidal and even autonomic signs Involvement of the inferior colliculi or their connections causes central deafness

Early compression of the aqueduct leads to fulminant hydrocephalus A state of decerebrate rigidity may occur similar to that seen in animals following section through the midbrain There is straightening and pro

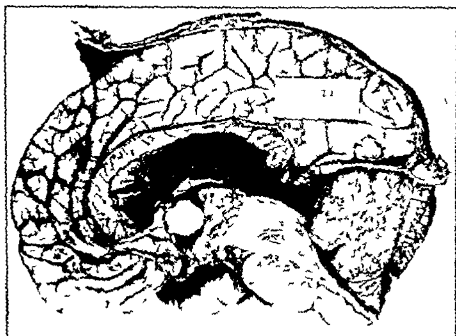


Fig 33 Encapsulated tumor of third ventricle which gave rise to hydrocephalus and to recurring autonomic seizures over a period of years (After Penfield 19 9)

nation of the arms stiffening of the legs and plantar flexion of the feet The neck is rigid but not opisthotonic Epileptiform seizures from the midbrain may be characterized by forced eye movements with loss of conjugate coordination There may be tonic seizures sometimes called cerebellar fits This syndrome usually is caused by infiltrating gliomas or by pineal tumors which compress the region[43]

In young boys pineal tumors often cause an endocrine disturbance with precocious puberty but this is lacking in the female and in adults of either sex It is probably due to compression of neighboring structures rather than to secretory activity of the tumor cells Horrax and Bailey[44] who studied 12 verified cases found oculomotor disturbance in 9 patients

and cerebellar signs in a similar number In 5 instances there was central deafness and 5 patients exhibited bilateral spasticity of the limbs Infiltrating tumors are of course inoperable but removal of pinealomas has been followed by good results for a period Meningeal fibroblastoma occasionally appears in this region attached to the falx

Syndrome of the Pons and Medulla

Tumors in this location early produce a kaleidoscopic variety of focal signs due to involvement of cranial nerve nuclei and important tracts They are responsible for many personalized syndromes which are better understood by a knowledge of anatomy than by a remembrance of names Infiltrating gliomas are remarkable in their production of florid focal symptoms with little or late evidence of increased intracranial pressure Papilledema appears in under 50 per cent of cases

The focal signs at first may suggest a lesion confined to one half of the brain stem but they soon become bilateral Oculomotor palsies occur early and there may be faulty conjugate movement of the eyes or pupillary abnormalities Incoordination and ataxia point to involvement of cerebellar pathways and weakness of the jaws loss of the corneal reflex or facial anesthesia signalizes trigeminal dysfunction Various types of crossed paralysis occur the commonest consisting of weakness of the face and jaw on one side and of the tongue soft palate and limbs on the other Unilateral or bilateral sensory changes may occur over the body and are of variable distribution There may be central deafness vertigo or nystagmus

Due to involvement of sympathetic pathways Horner s syndrome may appear and there may be flushing or sweating over the head neck and upper chest Finally there may be bilateral paralysis of bulbar muscles and limbs and disturbances of heart rate and respiration due to involvement of medullary centers

Tumors infiltrating the brain stem are of course inoperable The diagnosis can be made with certainty by careful encephalography to demonstrate the fourth ventricle and aqueduct of Sylvius as previously described in this chapter After such proof the patient can be spared operation

It should be remembered that metastatic tumors in the base of the skull may invade this region and also malignant retropharyngeal tumors The latter sometimes can be recognized by examination of the nasopharynx Chordomas growing from the basisphenoid are a rare cause of this syndrome[1 5]

Differential Diagnosis

Only brief mention can be made here of conditions which may simulate brain tumor They are dealt with at length in other chapters of this work

Cerebral abscess usually is associated with a recognizable focus of infection e g chronic mastoiditis acute otitis acute sinusitis peritonsillar abscess osteomyelitis of the skull or suppurative processes elsewhere in the body such as lung abscess or septicemia Its onset is apt to be acute or subacute and associated with some degree of fever leucocytosis signs of meningeal irritation or increased cell count in the cerebrospinal fluid Occasionally however the onset of cerebral symptoms is gradual and the original focus may be latent unrecognized or healed In such instances the signs of infection are lacking the cerebrospinal fluid may show no reaction and the signs and symptoms of the expanding lesion are indistinguishable from those of tumor Chronic abscess may be present for years and the brief acute symptoms of its onset be forgotten by the patient A meticulous history and painstaking search for foci of infection are of obvious importance

Subdural hematoma is relatively easy to recognize when acute and the result of severe head injury A slowly forming hematoma may occur however especially in the aged from trivial injury or no apparent injury and the course then is apt to be slowly progressive but with marked fluctuation of symptoms from day to day or week to week Headache drowsiness mental confusion and signs of increased intracranial pressure may wax and wane Compression of the hemisphere over a wide area may cause but few focal signs although some evidence of hemiplegia is apt to appear and aphasic defects too if the dominant hemisphere is involved Transient ocular palsies and inequality of the pupils are common but papilledema often is absent The cerebrospinal fluid usually shows no abnormality Chronic hematoma occurs more frequently with increasing age is much commoner in men than women and is bilateral in about half the cases The diagnosis is established by pneumography or by tapping the accumulation through burr holes in the frontal and parietal regions

Arachnoiditis meningitis circumscripta serosa may be indistinguishable from cerebral tumor until revealed at operation The generalized form obstructs the cerebrospinal fluid pathways and causes progressive and rather rapid increase of intracranial pressure without focal signs Localized arachnoiditis occurs most frequently at the base of the brain and in the lateral recess of the posterior fossa and thus may be responsible

for the suprasellar or cerebello pontine angle syndromes Subdural effusion of fluid due to inflammation in the region of the mastoid sometimes gives a picture resembling cerebral tumor

Cerebral vascular disease especially spreading thrombosis or softening due to ischemia may cause focal signs that are sufficiently slow in development to suggest tumor This is especially so since glioblastoma in elderly people often grows with great rapidity Such vascular lesions usually begin or are punctuated with an episode suggesting a slight stroke There is evidence of arteriosclerosis elsewhere especially in the retina the blood pressure often is elevated and papilledema is either slight or absent Tumor may of course be present in a patient with cerebral arteriosclerosis and pneumography is sometimes necessary to establish the nature of the lesion Cardiovascular renal disease and uremia may be the cause of headache vomiting cerebral symptoms and retinal changes which resemble those due to tumor The history abnormalities of urine and blood chemistry presence of vascular hypertension and the character of the eye ground changes usually point to the correct diagnosis

Neurosyphilis especially the meningo vascular form sometimes gives rise to papilledema symptoms of increased intracranial pressure and focal signs The progressive mental changes and epileptic seizures of dementia paralytica may suggest frontal lobe tumor Characteristic pupillary abnormalities usually are present however and serological reactions are positive Operation should never be attempted until the protean manifestations of syphilis have been excluded by tests of the blood and when safe of cerebrospinal fluid drawn from the lumbar sac Syphilis and cerebral tumor sometimes coexist and if clinical judgment points to tumor operation should not be long delayed if a brief trial of antiluetic therapy has achieved nothing

Intracranial aneurysm is apt to compress neighboring structures and when rupture or leakage has not occurred may simulate tumor Slow enlargement of the lesion causes progressive focal signs but increase of intracranial pressure scarcely ever occurs Much more often there are sudden episodes of increase in focal signs especially ocular palsies due to leakage from the aneurysm or the picture may be that of frank subarachnoid hemorrhage with severe headache stiffness of the neck photophobia and presence of blood in the cerebrospinal fluid Increased intracranial pressure and papilledema may of course occur during such episodes A careful history often reveals past incidents e g sunstroke bilious headache etc that suggest mild subarachnoid hemorrhage Such episodes are rare with brain tumor (see Russel and Kershman[107]) Aneurysm

usually is recognized on clinical grounds but cerebral arteriography may be necessary to establish the diagnosis or to determine the possibilities of surgical treatment

Disseminated sclerosis is unlikely to be confused with cerebral tumor but we have known confusion to occur especially during a bout of retrobulbar neuritis when the changes in the optic discs may be similar to or identical with those of true papilledema The visual impairment usually is very marked however and the defect involves central vision while the peripheral fields may be intact Central and paracentral scotomata are often present Headache and other signs of increased intracranial pressure are lacking though there may be pain behind the eyeballs Close questioning usually reveals the past occurrence of fleeting symptoms so characteristic of this disorder e g *mistiness of vision diplopia speech defect giddiness bladder dysfunction or variable numbness in an extremity On examination there is usually evidence of multiple lesions in the nervous system as* shown perhaps by dysarthria nystagmus *intention tremor or signs of* spinal cord involvement such as absent abdominal reflexes Babinski s sign hyperactivity of deep reflexes or defect of vibration and posture sense in the extremities

Other conditions may on occasion simulate tumor *Encephalopathy* due to lead poisoning may be associated with increased intracranial pressure and papilledema and there may be focal signs and epileptiform convulsions The history of possible exposure to lead the fulminant course colic vascular hypertension signs of renal damage evidence of peripheral lead palsy e g wrist drop and a lead line on the gums or a significant degree of basophilic stippling of red blood cells are all points of importance

Encephalitis periaxialis diffusa Schilder s disease occurs usually in childhood and may cause temporary papilledema There is widespread demyelinization of the white matter in the hemispheres with progressive blindness amentia epileptiform convulsions aphasia and signs of pyramidal tract damage The *evidence of very widespread and bilateral involvement usually excludes tumor and increase of intracranial pressure is never marked or of long duration*

Tuberculosis and other *more rare granulomas* as well as parasitic cysts often behave in the brain as true neoplasms and their identity may not be learned until operation They do not fall within the scope of this chapter and are dealt with elsewhere The differential aspects of epilepsy and migraine in relation to cerebral tumor are discussed in previous sections of this chapter

Morbid Anatomy

The signs and symptoms of brain tumor depend upon the expansion of the lesion and there may be little to indicate the nature of the growth whether benign or malignant Prognosis depends upon the histological nature of the growth and upon its location

Encapsulated Tumors

Under this heading are included the common benign tumors of the intracranial cavity which make up about one third of all so called brain tumors They find origin in the membranes which envelop the nervous tissue meningeal fibroblastomas from the meninges perineurial fibroblastomas from the sheath of the acoustic nerve and neurofibromas arising within any of the cranial nerves as a manifestation of von Recklinghausen s disease

Structure of Meninges — The meningeal covering of the brain is derived from perimedullary mesenchyme[124] At about the time that cerebrospinal fluid is first formed the meninx is differentiated into two layers the dura mater and the pia arachnoid Within the meshwork of the pia arachnoid the cerebrospinal fluid circulates The pia thus forms the true and most intimate investment of the nervous tissue The arachnoid layer remains less differentiated than the other layers being composed of cuboidal cells which tend to be heaped up in nests or pacchionian granulations As pointed out by Mallory[7] the cells of the dura differentiate to form collagen and elastic tissue fibrils as well as fibroglia while in the arachnoidea only fibroglia fibrils are found The presence of these fibrils is excellent evidence in favor of identifying the cells of both layers as fibroblasts which are differentiated to a lesser and greater extent

Structure of Perineurial Sheath — The cranial nerves are invested with a covering analogous to the pia arachnoidea which is also fibroblastic and which may be arbitrarily separated into an epineurium surrounding the whole nerve a perineurium about the nerve bundles and a still more intimate covering about each nerve fiber or endoneurium It should be remembered that the sheath of Schwann is quite different The Schwann cells are analogous to the neuroglia of the central nervous system and the Schwannian sheath lies between the endoneurium and the myelin sheath The fibroblasts of the perineurium including epi and endo neurium differentiate a little differently from those of the dura In the perineurium are to be found long wire like fibrils composed of reticu

lin These fibrils which are analogous to collagen sometimes referred to as pre collagen lend tensile strength to nerves as a whole

Meningeal Fibroblastoma (*dural endothelioma psammoma meningioma*) — This is a benign neoplasm which may be found anywhere



Fig 34 Frontal section of brain to show meningeal fibroblastoma arising from under surface of dura at site of pacchionian granulation Note that it pushes brain before it and that adjacent hemisphere has migrated under falx to opposite side The patient had been treated for years as an epileptic until she died during a seizure All the while the cause of her trouble was this easily removable tumor A similar tumor is shown in figure 3 during removal

in the cranial cavity attached to the dura mater It infiltrates the dura but pushes the brain before it (Fig 34) The tumor is covered by a connective tissue capsule and often is reddish when disclosed at operation On transection it is firm and finely granular It is at times degenerated and softened at the center but does not become cystic

These tumors are found most often in the vicinity of the dural sinuses particularly at the vertex and they sometimes grow into the sinus itself They appear most often in middle age being quite rare in the first and second decades

Morbid Anatomy

The signs and symptoms of brain tumor depend upon the expansion of the lesion and there may be little to indicate the nature of the growth whether benign or malignant Prognosis depends upon the histological nature of the growth and upon its location

Encapsulated Tumors

Under this heading are included the common benign tumors of the intracranial cavity which make up about one third of all so called brain tumors They find origin in the membranes which envelop the nervous tissue meningeal fibroblastomas from the meninges perineurial fibroblastomas from the sheath of the acoustic nerve and neurofibromas arising within any of the cranial nerves as a manifestation of von Recklinghausen s disease

Structure of Meninges — The meningeal covering of the brain is derived from perimedullary mesenchyme[1, 4] At about the time that cerebrospinal fluid is first formed the meninx is differentiated into two layers the dura mater and the pia arachnoid Within the meshwork of the pia arachnoid the cerebrospinal fluid circulates The pia thus forms the true and most intimate investment of the nervous tissue The arachnoid layer remains less differentiated than the other layers being composed of cuboidal cells which tend to be heaped up in nests or pacchionian granulations As pointed out by Mallory[7] the cells of the dura differentiate to form collagen and elastic tissue fibrils as well as fibroglia while in the arachnoidea only fibroglia fibrils are found The presence of these fibrils is excellent evidence in favor of identifying the cells of both layers as fibroblasts which are differentiated to a lesser and greater extent

Structure of Perineurial Sheath — The cranial nerves are invested with a covering analogous to the pia arachnoidea which is also fibroblastic and which may be arbitrarily separated into an epineurium surrounding the whole nerve a perineurium about the nerve bundles and a still more intimate covering about each nerve fiber or endoneurium It should be remembered that the sheath of Schwann is quite different The Schwann cells are analogous to the neuroglia of the central nervous system and the Schwannian sheath lies between the endoneurium and the myelin sheath The fibroblasts of the perineurium including epi and endo neurium differentiate a little differently from those of the dura In the perineurium are to be found long wire like fibrils composed of reticu

Histology of Meningeal Fibroblastoma — The nuclei are typically rounded or oval (Fig 35) but they may be elongated They tend to be found in whorls and calcareous deposits or psammoma bodies frequently are present The whorls the psammoma bodies and nuclear shape all produce an appearance strikingly like that seen in sections of pacchionian granulations as first pointed out by Schmidt[108] Indeed it is likely that the tumors take origin in such granulations

A pacchionian granulation is in fact a cluster of arachnoidal cells and penetrate the dural sinuses where they are believed to make possible the passage of cerebrospinal fluid from beneath the arachnoidea into the blood stream A meningeal fibroblastoma results from a pathological continuation of this invasion of the dura which is normally only a physiological process A meningeal fibroblastoma therefore is made up of meningeal cells from the less differentiated and avascular arachnoidea These cells invade the dura mater and receive their vascularization from this latter membrane

That the cells are little differentiated fibroblasts is borne out by the fact that fibroglia fibrils may be stained in their cytoplasm as shown in the whorl in Fig 35 There is also formation of collagen but not of elastic tissue fibrils according to Mallory

These tumors vary in rapidity of growth Some are quite cellular differentiate little form few whorls and even contain mitotic figures These are the less differentiated and more rapidly growing neoplasms which Bailey would call mesothelial meningiomas

In other more slowly growing tumors whorls are frequent and psammoma bodies numerous as in spinal meningeal fibroblastomas The cells of the tumor invade the dura and occasionally enter the Haversian canals of the overlying bone When the bone is involved the effect is a curious one Instead of eroding and thinning the bone as would be expected of most neoplasms this tumor produces hyperostosis New bone is laid down and heaps up chiefly on the outer table until a bony horn may appear as shown in Fig 36[99 90] More often the only attachment is to the dura from which the neoplasm may hang like an apple pushing brain before it (Fig 34) Rarely these tumors may spread out upon the under surface of the dura like a carpet

Treatment of Meningeal Fibroblastoma — Operation is the only treatment for these tumors They are not influenced by roentgentherapy Complete removal is followed by cure without recurrence but removal may be very difficult because of attendant blood loss or because of the position of the tumor deep under the brain As one of the sites of election is the falx and the region of the longitudinal sinus complete removal

Trauma is often a predisposing cause of the growth of these tumors We have observed a case in which a miner received a blow from a piece of coal Not long afterward symptoms of cerebral neoplasm made their appearance and subsequently a meningeal fibroblastoma was removed by one of us (W P) from within the cranial cavity at a point just beneath



FIG 35 Microphotograph of meningeal fibroblastoma Note fibrillar structure of cytoplasm in whorl Mallory s phosphotungstic acid hematoxylin stain

the blow as proven by the presence of carbon particles in the scalp Another such example is a case in which a meningeal fibroblastoma was found growing from the margin of a cranial defect previously produced by a depressed fracture of the skull This latter example was demonstrated to one of us by Dr F M R Walshe

Histology of Perineurial Fibroblastoma — The nuclei are irregularly elongated and tend to be arranged in palisades (Fig 39) or they may stream through the tissue as though influenced by a current The reason for this tendency to parallelism of arrangement of the nuclei is the



Fig 37 E P Operative photograph of meningeal fibroblastoma attached to dura at midline being turned out of its bed in the brain Note the adjacent daughter tumors also attached to under surface of dura to which artery clamp is attached

presence of bundles of long parallel wire like fibrils (Fig 40) When bundles of these fibrils intersect the nuclei are crowded to either side of the intersection producing an appearance of nuclear palisading (Fig 39)

The fibrils just described which are composed of reticulin are the

may necessitate ligation and removal of a portion of the sinus They are apt to spread along the dura as in Fig 37 which necessitates removal of the dura well outside of the attachment

Perineurial Fibroblastoma (neurinoma neuroma, etc) —These tumors are found growing from the sheath of the acoustic nerve The place of

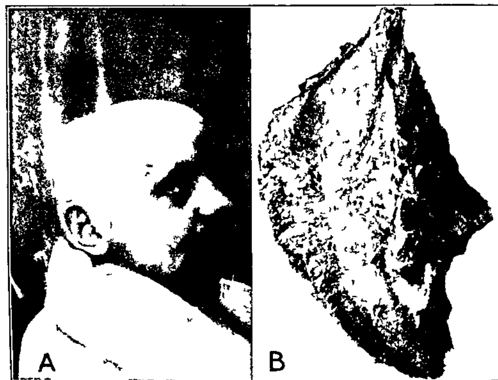


Fig 36 *A* Meningeal fibroblastoma invading frontal bone to form hard boss Note large artery in scalp *B* The bony horn has been sawed in half to show tumor infiltration and new bone formation A roentgenogram of similar case is shown in figure 11 (Patient operated upon by Sir Victor Horsley and case published by Penfield 19 3)

origin is said to be at the termination of the glial sheath In the case of this nerve the sheath extends outward from the medulla about 13 mm or to the entrance of the nerve into the internal auditory meatus Origin of these tumors from other cranial nerves is quite rare

The tumor itself is enclosed within a connective tissue capsule and there is often a loculated cyst of cerebrospinal fluid lying in the cerebello pontile angle over it Some examples are of firm consistency while others contain numerous small cysts due to irregular degeneration (Fig 38) These degenerating cystic tumors are apt to be soft and yellowish in color when opened

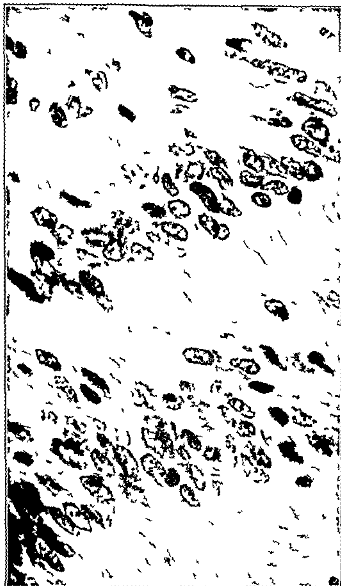


FIG 39 Microphotograph of perineurial fibroblastoma. Note palisading of nuclei

distinguishing feature of these tumors and indicate that the type cell is in reality a specialized fibroblast as pointed out by Mallory The fibrils may best be stained by silver For example, the method of Laidlaw[69] demonstrates them selectively This method may be used also to stain fibrils of the same type running in the perineurium of normal nerve sheaths In areas of softening curious degenerating cell forms may appear and many fat laden macrophages Nerve fibers may be found running in the sheaths of these tumors but not through tumor substance

Treatment of Perineurial Fibroblastoma is surgical as these neoplasms are not radio sensitive Removal sometimes must be partial because of their large size and because they are placed deep in the cerebello pontile angle In such cases the central softened portion is curetted out and the capsule left behind With such treatment recurrence occurs in a few years Complete removal often is advisable but it can only be carried out by sacrificing the facial as well as the acoustic nerve Only in the case of very small tumors the facial nerve may be spared But if it is cut anastomosis of the hypoglossal to the facial nerve in the neck may be carried out a week or two after tumor extirpation with satisfactory results



Fig 38 Perineurial fibroblastoma cut across to show small degenerative cysts (After Penfield 1932)

Neurofibroma of von Recklinghausen s Disease — These tumors are one manifestation of a diffuse affection which tends also to produce widespread thickening of nerves and pigmentation of the skin Neurofibromas are found more frequently upon peripheral nerves than centrally upon nerve roots On the other hand perineurial fibroblastomas are more frequently central than peripheral

In gross appearance the neurofibroma usually is a white shining encapsulated tumor attached like an anemic grape to a nerve root It is often degenerated and filled with a gelatinoid material

The thickening of nerves in this disease resembles a reactive process such as might result if the nerve fibers were improperly sheathed and therefore produced a connective tissue reaction like that in an amputation neuroma Similarly in the neurofibroma much of the tissue has a mixed fibrous formation (Fig 41) This is the mixed structure of Antoni[3] In other areas the histological appearance is quite typically that of a perineurial fibroblastoma Antoni s pure neurinoma as though the irritation which had produced the diffuse connective tissue reaction had in certain areas produced also true neoplastic growth These areas of

Pituitary Adenomas

Pituitary adenomas are of three types chromophobe chromophile and basophile depending upon whether the type cell resembles the chromophobe cell of the pituitary gland the acidophile or the basophile In the first group endocrine manifestations depend upon destruction of the pituitary gland by compression while chromophile adenoma produces within itself the hormone or hormones responsible for gigantism and acromegaly and the basophile adenoma is said to elaborate a hormone which produces the manifestations of Cushing s disease These have been discussed too in the previous section of this chapter



FIG 41 Neurofibroma from peripheral nerve in case of von Recklinghausen s disease Note patternless mixed structure (After Penfield 193)

Pituitary tumors arise within the sella turcica and beneath the dural diaphragm which roofs the sella On very rare occasions an adenoma of the pituitary may be derived from a rest of the craniopharyngeal pouch

fibroblastoma contain typical palisading of nuclei and parallel reticulin fibrils as described above

The most helpful differentiating point between neurofibroma and perineurial fibroblastoma is the fact that with appropriate stains nerve



FIG 40 Microphotograph of perineurial fibroblastoma of acoustic nerve Note typical wire like fibrils in parallel bundles stained by Laidlaw s silver method (After Penfield 1932)

fibers are found to pass through the tumor tissue of the former (Fig 42) whereas in the latter tumor the nerve is found ordinarily in the capsule The areas of degeneration are apt to contain clear jelly like material and bizarre degenerating nerve forms Fat filled macrophages such as are seen in perineurial fibroblastomas usually are absent

compressed and squeezed against the sellar wall until its function is gradually decreased with consequent appearance of clinical hypopituitarism

Treatment of the hypophyseal adenoma calls for both roentgentherapy and operation The transphenoidal operation of Hirsch has been largely abandoned and transfrontal hypophysectomy has taken its place This consists in elevation of the frontal lobe and incision of the diaphragm of the sella turcica which is found bulging upward beneath the optic chiasm The tumor is then curetted out but a complete removal is not possible and the hypophysis itself often is thus removed in part Radiotherapy gives satisfactory temporary results and should precede or follow operation

Chromophobe adenoma is the commonest of the pituitary neoplasms The type cell of the neoplasm is said to resemble the chromophobe cell of the pituitary gland but the neoplastic nuclei are larger and less pyknotic (Fig 43) The nuclei are irregularly round The chromatin net is fine with thickenings of considerable size

The cytoplasm does not contain specific granules of the chromophile cells The cellular arrangement may be alveolar as in the gland when there is apt to be a considerable connective tissue stroma On the other hand alveolar structure and stroma may be absent when the neoplastic cells are apt to resemble lymphocytes as pointed out by Dott and Bailey[8] This appearance has resulted in the name of chromophobe struma Colloid material may appear within the alveoli or among the cells Acidophilic cells do occur but are rare

These tumors usually are of solid consistency and they may be quite tough like muscle in appearance and consistency They occasionally become cystic but much less often than hypophyseal duct tumors

Chromophile adenomas contain eosinophilic or acidophilic cells in the cytoplasm of which are to be found specific alpha granules There are also present other cells of the chromophobe variety But it is the above acidophilic cells which are believed to produce growth and other hormones which result in gigantism and acromegaly These tumors may grow to large size and may become cystic but do not metastasize They occur less than half as often as chromophobe adenomas

Basophile adenoma was described more recently by Cushing[24] as a separate entity capable of producing the clinical syndrome of pituitary basophilism characterized by adiposity polycythemia hypertension skeletal changes and amenorrhoea or impotence

These tumors are very rare and it must be admitted that adenomas of this type have been reported without the above clinical manifestations The type cell is the basophilic or cyanophilic cell of the pituitary which

parahypophysis of Dandy which may be placed anywhere between hypophysis and pharynx and thus within the cranial cavity or even within the sphenoid bone As these intrasellar tumors enlarge they distend the sella turcica thus producing a tension which is responsible for the typical bitemporal headache Roentgenograms indicate that the sellar walls gradu



FIG 42 Neurofibroma in case of von Recklinghausen s disease Note nerve fiber with sheath cell upon it passing through tumor tissue (After Penfield 1932)

ally yield producing progressive enlargement and deepening of the sella (Fig 12)

Extension may occur into the underlying sphenoid sinus or a rupture through the sellar diaphragm may allow invasion of the intracranial chamber Upward extension either with or without rupture of the diaphragm produces as its primary result compression of the overlying optic chiasm which results in bitemporal hemianopsia If the neoplasm extends through the diaphragm it is apt to envelop one or both optic nerves

During this intrasellar neoplastic growth the pituitary gland itself i

The connection with the pharynx develops into a tube the hypophyseal tube which progressively atrophies and disappears at an early stage But rests of epithelial tissue may remain in the course of the former hypo physeal duct These rests occur within the sella or above it within the cranial cavity for the duct while it existed curved upward from the hypophysis forward and downward to the pharynx[19]

Thus these tumors are *found most frequently in the infundibulum* above the sella and next most frequently beneath the capsule of the an terior lobe of the pituitary Hypophyseal duct epitheliomas usually are cystic *They rise up into the position of the third ventricle and frequently* are calcified (Fig 10)

Histologically they are easily recognized by the presence of epithelium *suggestive of the pharynx* (Fig 44) *Calcium deposition and even bone* formation often are present There may be a close resemblance to ada mantinoma of the jaw and sometimes a teratomatous appearance *Al though very slow growth is the rule rapid growth with appearance of* mitotic figures occurs exceptionally At times a simple cyst only is found with little or no solid growth The fluid within the cyst is yellow and *high in albumen content It often contains cholesterin* crystals which lend an oily opalescent appearance to the fluid

The symptomatology of these neoplasms is of course that of destruc tion of the pituitary and of pressure upon the optic chiasm and optic nerves as in the case of chromophobe adenoma These tumors more often occur in children than do the adenomas and they are more apt to force their way up into the diencephalon

The treatment is partial surgical removal or aspiration of the cyst Roentgentherapy is useless

Papillomas of the Choroid Plexus

These rare neoplasms properly should be grouped with the gliomas They grow within the ventricles arising from the choroid plexus and may *infiltrate the brain as well They may be recognized easily because of* their resemblance to the choroid plexus The general arrangement is papillomatous with epithelial cell formation upon connective tissue stroma *For a review of the literature of these tumors see* Davis and Cushing[34]

Hemangioblastomas and Hemangiomas

Hemangioblastomas are true neoplasms arising from angioblastic cells in connection with the blood vessels of the brain They occur in the great

contains specific basophilic granules or beta granules of Bailey and Davidoff[3] Most investigators conclude that both acidophilic and basophilic cells are derived from the less differentiated chromophobe cells

Adenocarcinoma of the pituitary capable of metastasis does occur but it is so rare as to deserve no more than passing mention in this chapter

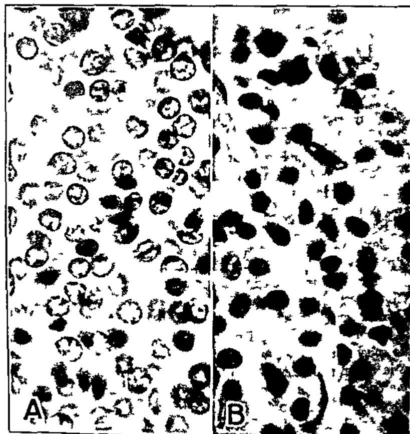


Fig 43 A Pituitary adenoma of chromophobe type B Anterior lobe of pituitary gland of same case and from same section Note different staining reaction and less pyknosis of neoplastic nuclei

Hypophyseal Duct Epitheliomas
(Craniopharyngiomas Adamantinomas Tumors of Rathke s Pouch)

These tumors arise in the region of the sella turcica and may grow to large size In embryo the anterior and intermediary lobes of the pituitary develop from an evagination of the pharyngeal wall called Rathke s pouch



FIG 45. *Hemangioma of parietal lobe photographed during operation The dura is being reflected from large veins which were filled with arterial blood entering longitudinal sinus above This patient came in complaining only of epileptiform seizures*

Hemangiomas may be taken to include congenital malformations of the blood vessels of the central nervous system The vessels vary in size from minute to huge vessels the size of one's finger (Fig 45 and see also

majority of cases in the cerebellum. Solid cellular collections may be present and blood formation may take place as in these tumors elsewhere. In the cerebellum they are often cystic. Often the cyst fluid formed by a hemangiomatous nodule collects about that nodule so that it



FIG. 44. Epithelioma of hypophyseal duct in child of ten. Note epithelial formation. (After Penfield, 1932.)

may seem at first inspection to be a simple cyst within the substance of the cerebellum. Actually the fluid is formed from the nodule situated in the cyst wall in a manner similar to the cyst formation of some cerebellar astrocytomas. Hemangioblastomas of the cerebellum are apt to be associated with small vessel collections in the retina and spinal cord and also with cysts of kidneys.[70]

found also within the ventricles where they seem to arise from the choroid plexus They have been reported not infrequently in this position in the ventricles of horses

Surgical removal gives satisfactory results but care should be taken to remove the sac as completely as possible

Chordomas (Chordoblastoma)

This is a rare tumor which seems to arise from a rest of the primitive notochord most often within the substance of the sphenoid bone It



Fig 46 Microphotograph of cholesteatoma found in cerebellopontile angle Note epithelial capsule (A) outside and epithelial scales (B) within

therefore appears at the base of the brain growing slowly and infiltrating the bone and floors of the cranial fossae

The cells are large their cytoplasm is voluminous and may contain vacuoles Mucin is apt to be present between the cells For a more complete description see Mallory[72]

Fig 27) Cerebral tissue will be found to lie between them, and although they are found usually on the surface they penetrate into the depths as well The vessels may be chiefly arterial or chiefly venous They are most frequent in the posterior portions of the cerebral hemispheres Occasionally only a red carpet of small vessels may be found upon the pia mater resembling somewhat birthmarks of the skin

These hemangiomas frequently do not give rise to symptoms until epileptiform seizures make their appearance or hemorrhage occurs There may be evidence of slowly advancing loss of cerebral function For an exhaustive study of the whole subject of intracranial hemangiomas and hemangioblastomas the reader is referred to Cushing and Bailey[2]

Arteriovenous aneurysms even when produced by trauma may come to resemble the congenital hemangiomas They tend to enlarge progressively involving an ever greater portion of the vascular tree of the brain

Treatment of hemangioblastoma of the cerebellum is most gratifying when radical surgery is employed the cyst evacuated and the hemangiomatous nodule extirpated Delay is dangerous as these patients sometimes die suddenly, due to bulbar compression The tumors themselves are no doubt sensitive to roentgentherapy but the fluid of the cyst cannot be influenced thus

The hemangiomas however can only be extirpated when they involve a relatively dispensable part of the brain such as the occipital pole for it is necessary to remove cerebral tissue in a block with the nest of vessels Intensive roentgentherapy may have to be employed in order to cause thrombosis of smaller vessels It has been our practice to remove the overlying bone leaving dura and scalp closed so as to allow more intensive radiotherapy This permits later surgical removal in case primary extirpation did not seem possible or advisable at the first operation

Cholesteatomas (Pearly Tumors)

A cholesteatoma consists of an epithelial sac within which is contained epithelial debris and cholesterin crystals which give to the tumor a pearly appearance The epidermis of the sac (A Fig 46) desquamates and the product of its desquamation (B Fig 46) gradually increasing in amount fills the sac to an ever greater size

Cholesteatomas not infrequently arise within the middle ear and perforate the dura mater after eroding the bone From here over a period of years they may grow to very large size within the subdural space

These tumors also are found at the base of the brain in relation to the meninges without any connection with the middle ear They may be

found also within the ventricles where they seem to arise from the choroid plexus They have been reported not infrequently in this position in the ventricles of horses

Surgical removal gives satisfactory results but care should be taken to remove the sac as completely as possible

Chordomas (Chordoblastoma)

This is a rare tumor which seems to arise from a rest of the primitive notochord most often within the substance of the sphenoid bone It



Fig 45 Macrophotograph of cholesteatoma found in cerebellopontile angle Note epithelial capsule (A) outside and epithelial scale (B) within

therefore appears at the base of the brain growing slowly and infiltrating the bone and floors of the cranial fossæ

The cells are large their cytoplasm is voluminous and may contain vacuoles Mucin is apt to be present between the cells For a more complete description see Mallory [3]

Sarcomas

Sarcomas arise in the dura mater and also in the pia. A *sarcoma of the dura* tends to erode the cranial vault and thus may present beneath the scalp after perforating the bone. These tumors do not infiltrate the bone or cause it to form a hyperostosis as the meningeal fibroblastomas sometimes do. They do not metastasize but tend to recur locally.

Histologically the cells vary a good deal in size. Collagen formation is irregular but sometimes voluminous. Mitotic figures are present. Careful search usually reveals small groups of cells resembling arachnoidal nests.[6]

Sarcomas of the leptomeninges also are rare. Because of their site of origin spread through the subarachnoid space is apt to occur producing a so called diffuse sarcomatosis. It is possible, of course, that such tumors may arise from the perivascular connective tissue within the brain and either from this source or from the intracerebral pial reflections sarcomas may be found apparently within the brain itself. Under such circumstances a single tumor may be encountered without diffusion. In the same manner meningeal fibroblastomas are found occasionally within the brain substance growing from leptomeninx or in the ventricle arising from the choroid plexus.

The histological structure[4] varies a good deal but the cells are apt to be rounded and little differentiated. Mitotic figures are numerous.

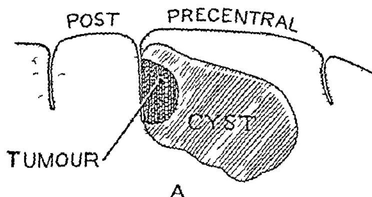
Melanotic sarcoma, also rare, may arise primarily from the leptomeninges, finding origin no doubt from the melanoblasts normally present in the pia mater at the base of the brain. They have histological characteristics similar to those of the melanotic sarcomas of the retina.

Metastatic Tumors of the Brain

Any tumor which metastasizes may do so to the brain but there is a special tendency for carcinomas of the bronchus to select the brain. Next in order of frequency are tumors of the breast, the urogenital system and the pigmentary structures.[4]

Metastatic neoplasms from sites outside the central nervous tissue, although they may grow within the brain, behave differently from gliomas. They seem unable to spread diffusely into cerebral tissue as though they found it unfavorable soil. These metastatic growths gain their vascularization from the meninges and are separated from the brain by a zone of softened cerebral tissue or even by cyst fluid (A, Fig. 47).

For this reason it is often quite simple to remove such growths as though they were encapsulated even from such areas as the motor gyrus.



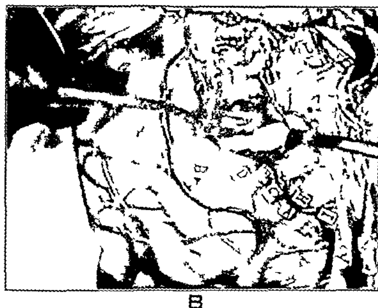


FIG 47 *A* Diagram of m tastatic carc noma from brea t seen in cross section to show its attachment to the fissure of Rolan lo From here t grew into the precentral gyrus from which it is separated by a collection of cystic flu d *B* The operative photograph shows the precentral gyrus etracted after removal of tumor and evacuation of cyst Small tickets nd cate sites along central fissure f om which electrical stimulation had elicited responses The ope ation was conducted under local anesthesia

as in the case illustrated in B Fig 47 and to relieve the patient from symptoms even for a year or two until death comes from other manifes tations of the malignant neoplasm

Tuberculomas Brain Abscesses and Syphilomas

These may give the signs and symptoms of a brain tumor Occasionally a brain abscess or even a tuberculoma may be removed successfully within its capsule These lesions however do not fall within the scope of this chapter

Subdural Hematoma (Pachymeningitis Hemorrhagica Interna)

Although this condition is not neoplastic it may simulate neoplasm to such an extent that description here is advisable

A subdural hematoma usually is the result of head trauma which may in some cases have seemed trifling An accumulation of blood occurs in the subdural space usually as the result of rupture of a tributary vein as it passes from brain to dural sinus It sometimes happens that the original hemorrhage gives rise to few if any symptoms initially As it remains in the subdural space there is formed about the blood clot a membrane which is thicker adjacent to the dura and thinner adjacent to the pia

The membrane beneath the dura becomes slowly organized and fibroblasts may grow into the clot to some extent Further hemorrhages may occur thus adding themselves to the clot sometimes as the result of further trauma But the striking thing about these clots is that they do not organize completely Instead they tend to liquify and as the result of this liquefaction a solution is formed capable of drawing fluid from the subarachnoid space through the pia and the thin pial membrane and thus insidiously increasing the total volume of the hematoma

Because of its moulded shape a hematoma is apt to give no indication of its local pressure Instead there are symptoms of increase of intracranial pressure or even signs of involvement of the opposite cerebral hemisphere because of displacement of the opposite cerebral peduncle against the incisura tentorii as at B in Fig 4

Treatment is of course surgical At times it suffices to drain the fluid contents through one or two trephine holes In other cases complete evacuation of the membranes is necessary The membrane upon the pia should be incised in any case to allow the brain to expand and thus to fill the dead space beneath the dura

Blood Cysts

Blood cysts within the brain may also result from trauma and even though they may be small at the beginning they may enlarge gradually

within a thin cyst wall the liquefied clot serving to increase the osmotic tension sufficiently to inflate the cyst over a period of years In a recent example of ours calcification occurred in the wall of a cyst resulting from a blow upon the head eight years previously Such intracerebral cysts are much less frequent than subdural hematomas

Gliomas

About 45 per cent of intracranial tumors belong to this group (Tooth 49 per cent Cushing 42 6 per cent Elvidge Penfield and Cone 45 per cent [117, 4, 6]) The name glioma originated with Virchow who recognized that these tumors were composed of neoplastic growth of the neuroglia cells Indeed previously it had been Virchow[1] who proposed the name neuroglia for the star shaped cells that he had concluded were not ganglionic

Description of Neuroglia — A brief description of neuroglia in the normal brain[90, 9] may simplify understanding of the gliomas Neuroglia is made up of astrocytes[15] and oligodendroglia[27] The astrocytes serve as supportive cells their multiple expansions being attached to the cerebral blood vessels by perivascular foot plates and thus the fibrous astrocytes bind these vessels together as by guy ropes into a vaso astral framework Oligodendrocytes are smaller very numerous cells which surround nerve cells and myelin sheaths and which doubtless play a rôle in the formation and maintenance of myelin

All neuroglial cells are developed from the primitive neuroepithelium (Fig 48) This epithelium contains neuroblasts which migrate outward to form neurones From the neuroepithelium also come spongioblasts which develop into astroblasts and astrocytes on the one hand and oligodendroblasts and oligodendrocytes on the other Microglial cells described by Hortega are potentially phagocytic cells and form no tumors

Classification of Gliomas — Tooth[117] studied the material derived from the surgery of Sir Victor Horsley and attempted to subdivide 258 verified intracranial tumors He failed to distinguish separate groups not having at that time knowledge of neuroglial forms Roussy L hermitte and Cornil[10] made a more effective effort and Bailey and Cushing[4] made a complete classification of 254 verified gliomas on the basis of the differentiation of the neuroglial type cell

The following outline is a simplification of that of Bailey and Cushing see also classification adopted by the American Neurological Association The percentage figures indicate the relative frequency of each subdivision

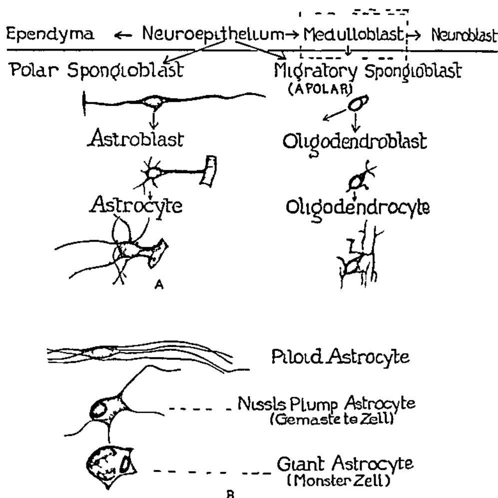


FIG 48 *A* Neuroglia development from neuroepithelium to adult astrocyte and oligodendrocyte *B* Pathological forms of astrocyte found in gliomas (After Penfield 1931)

in a series of 210 histologically verified gliomas of the brain and spinal cord reported by Elvidge Penfield and Cone[45]

Astrocytoma — Most of the brilliant surgical results in the treatment of gliomas fall in this group Astrocytoma is an infiltrating tumor which is found most often in the cerebrum but also about half as frequently in the cerebellum When in the cerebral or the cerebellar hemispheres the average age of patients is the fourth decade when in the midline of the cerebellum the average age is in the first decade

Preoperative history usually is long from one to five years Post operative survival should be long also although a very deep astrocytoma

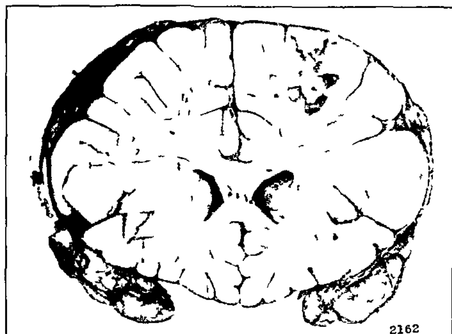


Fig 49 Astrocytoma of cerebral hemisphere (gemistocytic type) Note widening of the overlying convolutions and decreased depth of fissure and replacement of cerebral structure also small cyst about nodule

may be considered as inoperable as a malignant neoplasm as pointed out by Cairns[14]

GLIOMAS

	Subdivision	*Percentage*
1	Astrocytoma	26
2	Glioblastoma multiforme	
3	Medulloblastoma	13
4	Ependymoma	9
5	Astroblastoma	6
6	Spongioblastoma polare	5
7	Oligodendroblastoma and oligodendroglioma	4
8	Neuroepithelioma	0 5
9	Pinealoma	1
10	Unclassified	10
		99 5

Astrocytoma infiltrates the brain growing slowly and usually appearing at the surface (Fig 49) where it produces marked widening of the infiltrated convolutions It produces pallor and decreased vascular markings of such convolutions as is shown in Fig 50

Histology —On histological grounds these tumors must be divided into three groups for proper understanding[96, 4]

Pilocytic astrocytoma (Greek pilos — hair wrought into felt) This

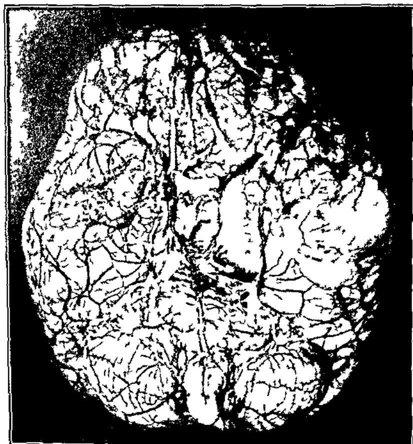


FIG 50 Astrocytoma of left temporal lobe Blanching of pia is quite characteristic.

tumor is made up largely of piloid astrocytes (see B Fig 48) It contains therefore many long fine neuroglial fibrils and scattered elongated nuclei There is frequent cyst formation and the cystic change is associated with liquefaction of the neuroglial fibers as indicated in Fig 51

Gemistocytic astrocytoma (from the Greek word gemistos meaning filled up) The type cell of this tumor is Nissl s plump astrocyte or ge

mastetc zell as shown in Fig 48 The cells contain a large amount of opaque cytoplasm the nuclei are often forced to the periphery and frequently are found to be multiple (Fig 52) The e tumors may also form

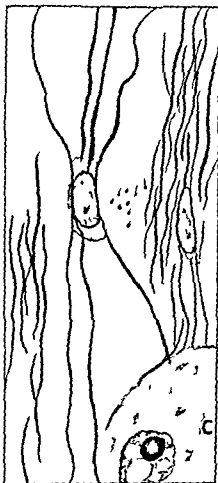


Fig 51 Cells of piloid astrocytoma Cystic degeneration at C. Note long slender neuroglial fibrils which liqu fy in cystic area

cysts as shown in Fig 49 although this is less frequent than in the pilocytic group

Astrocytoma diffusum This is a diffusely infiltrating neoplasm found in the cerebral hemisphere of adults The type cell is a small astrocyte

resembling the astrocyte of normal brain tissue (Fig 53) The nuclei are rounded of equal size and are found diffusely scattered through the brain (Fig 54) Perineuronal satellites are apt to be greatly increased in number especially near the frontier of the tumor as though an extra

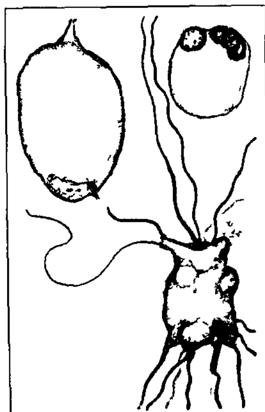


Fig 5 Cells from gemistocytic astrocytoma Note increased amount of opaque cytoplasm and multiplication of nuclei

neoplastic influence had caused these cells to multiply in situ and themselves to become neoplastic Mitotic figures may be found in such widely scattered neoplastic cells

There is practically no demarcation to be found between tumor and cerebral tissue either at operation or on histological examination Nerve cells are displaced by the diffuse infiltration and perhaps by migration of the neoplastic cells so that they are found at a distance from their proper grey layers The neurone displacement may also be associated with some change in the cell appearance so that this tumor has been mistaken for a combined neuroblastic and spongioblastic neoplasm Because of its dif

fuse growth and the preservation of neurones this tumor may cause little or no obvious disturbance of function even when the volume of tumor is large (Fig 55)

Astrocytoma diffusum is less frequent than the piloid and gemistocytic types 9 out of 55 astrocytomas

The astrocytomas grow slowly Both gemistocytic and piloid types may be well demarcated but are never encapsulated Radical removal should result in years of freedom from symptoms Even permanent cure may result from radical removal of cystic pilocytic astrocytomas of the cerebellum

The *pilocytic astrocytomas* make up over half of the group (29 out of 55) They are the most benign and most frequently cystic They occur most often in the cerebellum but also in the cerebrum They are usually quite firm in consistency unless degenerating

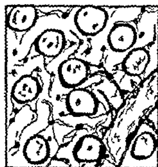


Fig 53 Cells of astrocytoma diffusum

The *gemistocytic tumors* 15 out of 55 occur in the cerebrum rather than in the cerebellum They are less often cystic but are easily removed being usually soft in consistency They recur more rapidly than the pilocytic tumors but may be removed successfully more than once

Astrocytoma diffusum 9 out of 55 occurs only in the cerebrum and forms no cysts except for occasional small ones It has no line of demarcation and may grow to large size and extend widely without interrupting cerebral function Its removal produces loss of function of course and should only be undertaken when the location is distant from vital centers as in the frontal or occipital poles

Roentgentherapy has little if any influence upon pilocytic astrocytomas It may have a moderately inhibiting effect upon the gemistocytic group Its effect upon the diffuse type has not yet been established over a long period but is definitely favorable for a short time

Glioblastoma Multiforme (Spongioblastoma Multiforme of Strauss and Globus 1918) —This is a rapidly growing tumor that arises most often deep in the cerebral hemisphere (Fig 56) although in rare cases it may be found in the brain stem cerebellum or spinal cord It is second in frequency only to astrocytoma forming 25 per cent of all gliomas In the hemisphere it appears usually in late middle age averaging 48 years In the brain stem and cerebellum it may occur in childhood

Histological examination demonstrates great multiformity of neuroglial cells in this tumor including numerous small migratory spongioblasts astroblasts astrocytes and giant astrocytes (see A Fig 57 and compare with Fig 48) If one were to choose a type cell the small spongioblast probably would be selected but multiformity of cell type is

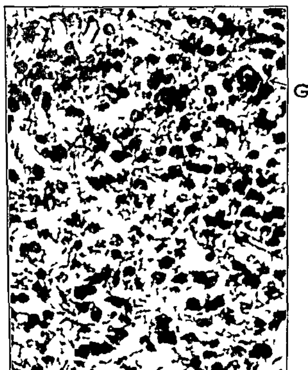


Fig 54 Microphotograph of astrocytoma diffusum Note included ganglion cells at G and elsewhere

the outstanding cytological characteristic of this tumor Mitotic figures are numerous both within the neuroglial neoplastic cells and within the cells of the blood vessels

Indeed the most striking feature of these tumors is the amazing overgrowth of the walls of the blood vessels This may occur either in the vascular epithelium or in the adventitia Thus glomeruloid buds appear (B Fig 57) containing new blood channels and obliterating old channels This fluctuation of blood supply no doubt accounts for the variability in the appearance of the neoplastic cell on the one hand and for the appearance of numerous small areas of degeneration scattered throughout the tumor Such degeneration may lie adjacent to areas of rapid cellular growth The diagnosis is made most easily by the discovery of vascular changes

such as those just described Cysts do occur in the areas of degeneration but they are small and apt to be multiple Spontaneous hemorrhages into the substance of the tumor are frequent

The course of these tumors is rapidly fatal as a rule From the first



FIG 53 *Photograph at operation Large astrocytoma diffusum greatly enlarging* the postcentral convolutions of left hemisphere This middle aged right handed man had no aphasia no paresis and no sensory disturbance Normal function was continuing despite tumor infiltration Tickets 1 to F indicate central fissure This operation was carried out before the Society of Neurological Surgeons Biopsy done and closure without removal

symptom to death *not* infrequently is only a matter of six or eight weeks but the average pre admission history is six months

Treatment depends upon the location *If* situated in a frontal or occipital pole or when superficially placed radical surgical extirpation may result in relief of symptoms for from six months to two years These tumors are moderately sensitive to radiotherapy and may be held in check

Histological examination demonstrates great multiformity of neuroglial cells in this tumor including numerous small migratory spongioblasts astroblasts astrocytes and giant astrocytes (see A Fig 57 and compare with Fig 48) If one were to choose a type cell the small spongioblast probably would be selected but multiformity of cell type is

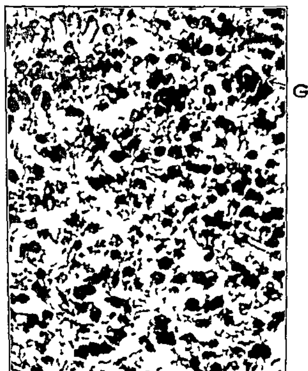


Fig 54 Microphotograph of astrocytoma diffusum Note included ganglion cells at G and elsewhere

the outstanding cytological characteristic of this tumor Mitotic figures are numerous both within the neuroglial neoplastic cells and within the cells of the blood vessels

Indeed the most striking feature of these tumors is the amazing over growth of the walls of the blood vessels This may occur either in the vascular epithelium or in the adventitia Thus glomeruloid buds appear (B Fig 57) containing new blood channels and obliterating old channels This fluctuation of blood supply no doubt accounts for the variability in the appearance of the neoplastic cell on the one hand and for the appearance of numerous small areas of degeneration scattered throughout the tumor Such degeneration may lie adjacent to areas of rapid cellular growth The diagnosis is made most easily by the discovery of vascular changes

such as those just described Cysts do occur in the areas of degeneration but they are small and apt to be multiple Spontaneous hemorrhages into the substance of the tumor are frequent

The course of these tumors is rapidly fatal as a rule From the first



FIG 59 Photograph at operation Large astrocytoma diffusum greatly enlarging the postcentral convolutions of left hemisphere This middle aged right handed man had no aphasia no paresis and no sensory disturbance Normal function was continuing despite tumor infiltration Tickets I to R indicate central fissure This operation was carried out before the Society of Neurological Surgeons Biopsy done and closure without removal

symptom to death not infrequently is only a matter of six or eight weeks but the average pre admission history is six months

Treatment depends upon the location If situated in a frontal or occipital pole, or when superficially placed radical surgical extirpation may result in relief of symptoms for from six months to two years These tumors are moderately sensitive to radiotherapy and may be held in check



Fig 56 Glioblastoma multiforme infiltrating cerebral hemisphere Note swelling of hemisphere decrease in size of adjacent ventricle and dilatation of opposite ventricle

by this means for a short time If situated deeply they produce enormous swelling of the hemisphere (see Fig 56) Under such circumstances it seems more charitable to remove a small biopsy specimen in a hollow needle through a trephine hole thus proving the nature of the lesion and then to allow the patient to die in a few days or weeks rather than to

render him hemiplegic and perhaps aphasic by a heroic operation so that he may drag out a miserable existence over a period of a year

Medulloblastoma (Gliosarcoma Neurospongioma of Roussy Oberling and Raileanu 1931) —This tumor as was first pointed out by Bailey and Cushing[7] is derived from the bipotential indifferent cell or medulloblast

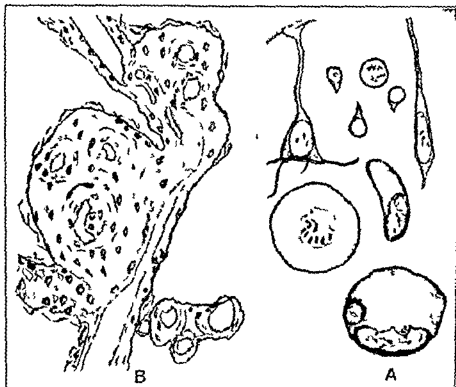


Fig 57 A Cells from glioblastoma multiforme Note variability of form from small spongioblast to giant glial cell Mitotic figures in both large and small cells *B* Overgrowth and obliteration of lumen of vessel

of the cerebellum It is found almost exclusively in the cerebellum although it frequently metastasizes through the cerebrospinal fluid In our experience it has never arisen outside of the posterior fossa It is most common in early life average age 19 oldest patient 50 youngest 4

Histologically these diffusely cellular tumors are easily recognized There are numerous pyknotic round or oval nuclei resembling lymphocytes These are sometimes arranged in columns and sometimes form

pseudorosettes as in Fig 58 There is also a scattering of less pyknotic nuclei which belong to the connective tissue stroma Mitotic figures are seen frequently

Ordinary paraffin stains are apt to leave the cytoplasm invisible, but when stained with silver carbonate the cells are seen to possess nipple

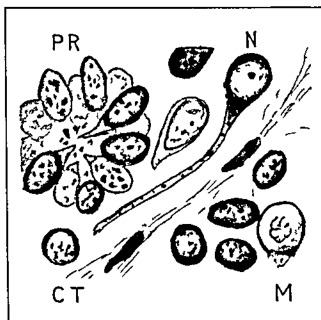


Fig 58 Cells from medulloblastoma PR pseudorosette CT connective tissue stroma M mitotic figure N neuroblast

like expansions In some cases well formed neuroblasts (N Fig 58) may be demonstrated The tumor cell thus is bipotential neurogenic and neurogliogenic just as is the medulloblast which migrates out from the medullary epithelium over the surface of the developing cerebellum[67]

The course of these tumors is rapidly fatal if nothing is done The average preoperative history in our cases was five months The secondary hydrocephalus due to the blockage of cerebrospinal fluid outflow at the aqueduct of Sylvius produces rapidly increasing pressure and sometimes sudden death

Operative extirpation should be complete and done in such a manner as to prevent spread through the spinal fluid One of our patients after removal of a medulloblastoma of the cerebellum survived nine years without symptoms before recurrence That this is the longest survival on record may be due to the fact that the preoperative diagnosis was ab

scess and unusual care therefore was taken to prevent contamination of the leptomeninges These tumors are very sensitive to roentgentherapy and may be made to melt away under its influence For this reason it has been urged[7] that radiotherapy be used without operation This method of treatment however will lead surgeons to miss cystic astrocytomas of the cerebellum which may be removed with brilliant result It is well however to follow careful extirpation with radiotherapy which should be directed to the operative site and to the whole of the cranial and spinal cavities Even then however complete recovery for two or three years is the best that ordinarily can be achieved

The remaining glioma types are relatively rare and although of great interest to the operating neurosurgeon will only be described briefly here

Ependymoma — Ependymoma is frequent among spinal gliomas but less so within the cranial cavity The location may be either in the cerebrum or cerebellum The average age of patients is 29 The rate of growth is moderate but the deep situation adjacent to a ventricle usually makes removal difficult

Histologically the one constant finding prerequisite to the diagnosis is some tendency to form ependymal epithelium often in rosettes The epithelial cell is apt to form a cilium and to contain small granules or blepharoplasten a short distance beneath the cell membrane (Fig 59) and peripheral cytoplasmic expansions may be found running outward There is differentiation into astrocytes and astroblasts within the tissue We have seen no mitotic figures in our cases

Astroblastoma — These tumors comprising 6 per cent of the gliomas occur chiefly in the cerebrum either deep or superficial Both anatomically and biologically they lie between benign astrocytoma and malignant glioblastoma

The type cell is the astroblast but as ordinary stains demonstrate the cytoplasm with the greatest difficulty it may be observed only that the neoplastic nuclei encircle the vessels at a considerable distance (Fig 60) from the vessel wall Connective tissue septa may also form a surface for the application of astroblastic foot processes Mitotic figures are frequent Not infrequently vessel overgrowth occurs in these tumors similar to that already described for glioblastoma multiforme Such vessel change which signifies its kinship to glioblastoma adds a comparatively bad prognosis

Spongioblastoma Polare — These tumors although rare are important of recognition because they are benign and give an excellent prognosis for long survival They may be cystic

Histologically they contain elongated cells (Fig 61) which sometimes

pseudorosettes as in Fig 58 There is also a scattering of less pyknotic nuclei which belong to the connective tissue stroma Mitotic figures are seen frequently

Ordinary paraffin stains are apt to leave the cytoplasm invisible but when stained with silver carbonate the cells are seen to possess nipple

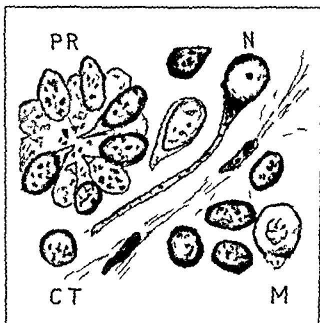


Fig 58 Cells from medulloblastoma PR pseudorosette CT connective tissue stroma M mitotic figure N neuroblast

like expansions In some cases well formed neuroblasts (N Fig 58) may be demonstrated The tumor cell thus is bipotential neurogenic and neurogliogenic just as is the medulloblast which migrates out from the medullary epithelium over the surface of the developing cerebellum[6]

The course of these tumors is rapidly fatal if nothing is done The average preoperative history in our cases was five months The secondary hydrocephalus due to the blockage of cerebrospinal fluid outflow at the aqueduct of Sylvius produces rapidly increasing pressure and sometimes sudden death

Operative extirpation should be complete and done in such a manner as to prevent spread through the spinal fluid One of our patients after removal of a medulloblastoma of the cerebellum survived nine years without symptoms before recurrence That this is the longest survival on record may be due to the fact that the preoperative diagnosis was ab

Histologically these neoplasms are easily recognized by the rounded nuclei laid together evenly almost in mosaic (B Fig 62) The stroma may be formed by numerous small astrocytes in an interesting way Calcium deposition is frequent even when the tumors are fairly rapidly

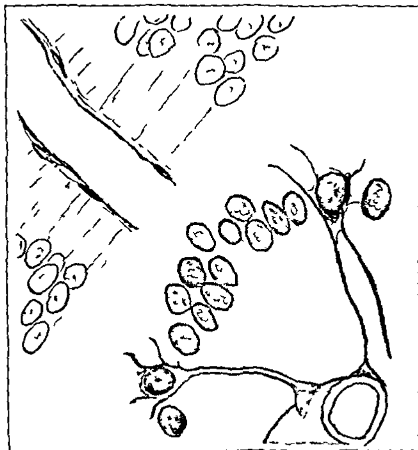


FIG 60 Cells from astroblastoma Note tendency of nuclei to be distant from vessels also two well stained astroblast

growing Usually there is little cytoplasmic differentiation as the cells are apt to remain in the oligodendroblast stage

Neuroepithelioma — This is an extremely rare tumor in the central nervous system It is malignant in its growth Histologically it contains neuroepithelial rosettes and numerous mitotic figures

are so attenuated as to resemble neuroglial fibrils Apparent fibrils in these tumors however will be found to be actually elongations of the cytoplasmic expansions as may be seen with the help of Mallory s phosphotungstic acid hematoxylin stain or Hortega s silver carbonate method



FIG 59 Ependymal ring from ependymoma Note cilia blepharoplasten peripheral expansions astrocyte

Treatment should be surgical extirpation There is no evidence that radiotherapy is of any benefit One of our patients is alive and quite well eight years after removal of such a neoplasm from the roof of the midbrain

Oligodendroblastoma and Oligodendroglioma — All of the tumors of this group in our series 8 in number were located in the cerebral hemispheres the average age being 37 years The preoperative history is long averaging 12 years In spite of this long preliminary course some of the tumors grow quite rapidly after removal The situation is cerebral and almost always superficial so that surgical removal is simple and safe

The chief advantage of subclassification is that it makes discriminative prognosis possible Glioblastoma multiforme is the most malignant of all gliomas and astroblastoma often behaves similarly Medulloblastoma also is practically certain of recurrence but if properly handled usually will give no symptoms for a period of from one to four years Astrocy

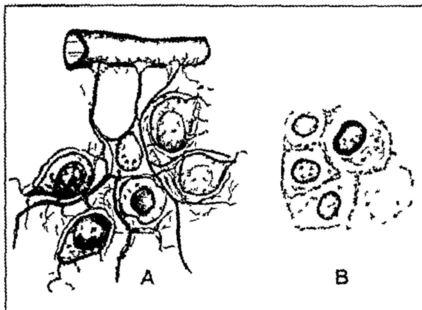


FIG 6 Case R I Cells from oligodendroglioma *A* Silver carbonate stain shows short expansions on oligodendrocytes The small astrocyte which is attached to vessel provides stroma for tumor tissue with its expansions *B* With hematoxylin and eosin stain or almost any paraffin method such halos about nuclei are seen in mosaic arrangement This tumor was partly calcified It had been present for , years before operation It recurred 18 months after operation and death occurred 6 months after second operation

toma of the piloid type often is very slow to recur and spongioblastoma polare as well *Oligodendroglioma* often extremely slow of growth and frequently calcifying is sometimes capable of a change of pace to rapid growth Ependymoma so slow in its evolution within the spinal cord is apt to grow a little more rapidly within the brain

Some tumors may present characteristics of two subgroups and classification must be made by some arbitrary rule such as calling any glioma an ependymoma if ependymal epithelium appears in it even though many microscopic fields resemble astrocytoma But after careful effort

Pinealoma — Also extremely rare this is a tumor that arises in the region of the pineal gland and gives rise to extreme hydrocephalus because of this position (Fig 63) The tumor may metastasize through the ventricles and cerebrospinal spaces as in Fig 63

Histologically it contains cells of two very different types large cells resembling pineal parenchyma with large spherical nuclei and smaller lymphoid cells (Fig 64)

The surgical removal is difficult because of its deep situation Removal should be followed by radiotherapy as the neoplasm is radiosensitive For further discussion of pinealoma the reader may be referred to Horrax and Bailey[64] and Globus and Silbert[54]

General Observations on the Gliomas

Certain characteristics are common to all the subgroups of gliomas They are capable of infiltrating brain tissue without throwing up a barrier Thus a glioma gives the histological appearance of being at home in the nervous tissue whereas as mentioned above a metastatic neoplasm expands within itself and is separated from the nervous tissue by a frontier of softened cerebral tissue or a connective tissue barrier

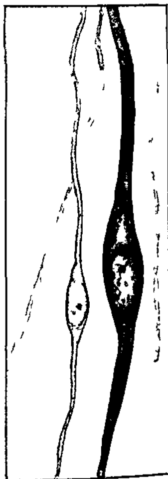


Fig 61 Cells from polar spongioblastoma Note that the expansions although of small caliber do not contain neuroglial fibrils as in figure 51

Gliomas do not metastasize by way of the blood stream and there are no lymph channels within the central nervous tissue for them to invade They may however spread within the subarachnoid space and may metastasize to a distance through the cerebrospinal fluid as pointed out particularly by Cairns and Russell[17] Such metastasis occurs most frequently from medulloblastoma but also from glioblastoma astroblastoma pinealoma and according to Cairns and Russell even from astrocytoma In the case of this last group it must be very rare indeed



Fig 64. Microphotograph of pinealoma (by kindness of Dr Cone) Note two types of cell

to classify all the gliomas there will remain in any large group certain examples between 5 per cent and 10 per cent at the present time which cannot be honestly classified and must be labelled unclassified gliomas

The initial cause of gliomas is not known There is no valid evidence that trauma is a factor in the inauguration of such neoplasms In this

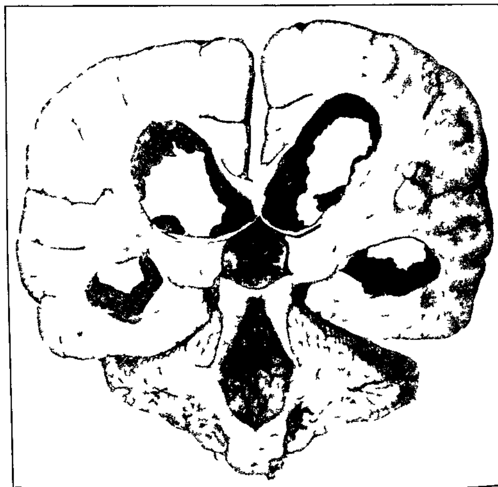


FIG 63 Pinealoma primary in pineal recess shown in frontal section of brain Note metastases in dilated lateral ventricles and metastatic growth filling the fourth ventricle Tumor was removed initially and the operation was followed by apparently complete recovery for one year Recurrence then held in check for a time by radiotherapy Same case as figure 23

regard they are quite different from meningeal fibroblastomas Gliomas are sometimes familial We have encountered four examples of glioma in brother and sister and one instance may be cited of a man who died at

9 BAILEY P and DAVIDOFF L M 19 5 Microscopic structure of hypoph s is cerebri in acromeg ly Am Jour Path 19 5 I 185
10 BECKMANN J W and KUBIE L S 19 9 A clinical study of twenty-one ca es of tumour of the hypophyseal stalk Brain 19 9 LII 127
11 BERGSTRAND H OLIVECRONA H and TÖNNIS W 1936 Gefassmissbildungen und Gefa geschwulste des Gehirns Thieme Leipzig 1936
1 BRAIN W R 1933 Disea es of the Nervous System Oxford Univ Pres 1933
13 BROUWER B 1930 Ueber die Projektion der Makula auf die Area striata de Menschen Jour f Psychol u Neurol 1930 XL 147
14 BROUWER B VAN DER HOEVE J and MAHONEY W 1937 A fourth type of phakomatosis Sturge Weber Kon akad Wet verhand (Tweede Sectie) 1936 XXXVI 1
15 BULLOCK L T GREGERSEN M I and KINNEY R 1935 The use of hypertonic sucrose solution intravenously to reduce cerebro pinal fluid pressure without a secondary rise Am Jour Physiol 1935 CXII 8
16 CAIRNS H 1936 The ultimate re ult of operations for intracranial tu mour a study of a series of cases after a nine year interval Yale Jour Biol and Med 1936 VIII 4 1
17 CAIRNS H and RUSSELL D 1931 Intracranial and spinal metastases in gliomas of the brain Brain 1931 LIV 3
18 CAJAL S RAMÓN y 1913 Contribucion al conocimiento de la neuroglia del cerebro humano Trab le Lab d Inv Biol d l Univ d Madrid 1913 XI 5
19 CONE W V and MACMILLAN J A 193 The optic nerve and papilla Cytology and Cellular Pathology of the Nervous System Vol III chapt XXII p 389 P Hoeber Inc New York 193
0 CUSHING H 1917 Tumors of the Nervu Acu ticus Saunders Phila 1917
1 CUSHING H 1930 The chia mal syndrome of primary optic atrophy and bitemporal field defects in adult with a normal sella turcica Arch Ophthalmol 1930 III 505 and 04
CUSHING H 193 Pituitary Body Hypothalamus and Parasympathetic Nervou System Cha C Thoma Baltimore 1932
23 CUSHING H 193 The bas phil adenomas of the pituitary body and their clinical manife tation Bull Johns Hopkins Ho p 193 L 13
24 CUSHING H 1932 Intracranial tumor Notes upon a series of two thou sand verified cases with surgical mortality percentage pertaining thereto Thomas Baltimore 193
25 CUSHING H and BAILEY P 19 8 Tumors Arising from the Blood Vessel of the Brain Angiomatous Malformations and Hemangiobla tomas Cha C Thomas Baltimore 19 8
6 CUSHING H 193 The surgical mortality percentages pertaining to a series of two thousand verified intercranial tumors Arch Neurol and P ychiat 1932 XXVII 1
7 CUTLER E C SOSMAN M C and VAUGHAN W W 1936 The pla e Vot XI 938

thirty six years having been operated upon by Dr Harvey Cushing for astroblastoma of the left temporal lobe He recovered temporarily but died from recurrence two years later His sister at the age of forty four was operated upon by one of us (W P) for an oligodendroglioma situated in the same region of the same hemisphere The tumor recurred and she died four years after operation This might seem to suggest a congenital rest as predisposing factor The type of glioma differed somewhat but the location was the same and the duration from initial epileptiform seizure until death was about the same in the two cases from seven to eight years

Treatment —Operation usually is the treatment of choice unless the position of the tumor makes this inadvisable Very radical extirpation gives more satisfactory results than so called conservative decompression or fearful partial removal The time has passed when palliative, subtemporal decompressions are justifiable except under the most exceptional circumstances The neoplasm can be localized and it should be removed and the skull closed Hernia cerebri after surgical procedures is an evidence of inadequacy or accident

The decision for or against operation often is a human problem rather than a strictly medical one Deep radiotherapy usually is carried out by roentgen ray It is most effective upon medulloblastoma but it also influences the other more rapidly growing gliomas as mentioned under each section It should follow operation and histological study

BIBLIOGRAPHY

1 ADSON A W KERNOHAN J W and WOLTMAN H W 1935 Cranial and cervical chordomas Arch Neurol and Psychiat 1935 XXXIII 247
2 AMERICAN NEUROLOGICAL ASSOCIATION 19 8 Classification of neurological psychiatric and endocrine di orders, New York
3 ANTONI N 1920 Ueber Rückenmarkstumoren und Neurofibrome, Bergmann Munchen 1920
4 BAILEY P 1929 Intracranial sarcomatous tumors of leptomeningeal origin Arch Surg 19 9 XVIII 1359
5 BAILEY P 1933 Intracranial Tumors Chas C Thomas Baltimore 1933
6 BAILEY P and BUCY P C 1929 Oligodendrogliomas of the brain Jour Path 1929 XXXII 735
7 BAILEY P and CUSHING H 19 5 Medulloblastoma cerebelli Arch Neurol and Psychiat 1925 XIV 192
8 BAILEY P and CUSHING H 1926 A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis J B Lippincott Phila 19 6

46 FRAZIER C H 1930 Cerebral pseudotumors Arch Neurol and Psychiat 1930 XXIV 1117

47 FRAZIER C H 1936 Tumor involving the frontal lobe alone A symptomatic survey of one hundred and five verified cases Arch Neurol and Psychiat 1936 XXXV 525

48 FRAZIER C H 1936 A review clinical and pathological of parahypophyseal lesions (Muetter Lecture) Surg Gynec and Obstet 1936 LXII 1 and 158

49 FRAZIER C H 1935 Fifty years of neurosurgery Arch Neurol and Psychiat 1935 XXXIV 90

50 FREMONT-SMITH F 1937 The cerebrospinal fluid in brain tumor A Res Nerv and Ment Dis Proc 1937 XVI 315

51 FREMONT-SMITH F and HODGSON J S 19[illegible] Combined ventricular and lumbar puncture in the diagnosis of brain tumor A Res Nerv and Ment Dis Proc 19[illegible] IX 1[illegible]

5 GARDNER W J and FRAZIER C H 1930 Bilateral acoustic neurofibromas Arch Neurol and Psychiat 1930 XXIII 266

53 GLASER M A 19[illegible]9 Tumour of the pineal corpora quadrigemina and third ventricle the interrelationship of their syndromes and their surgical treatment Brain 19[illegible]9 LII 2[illegible]6

54 GLOBUS J H and SILBERT S 1931 Pinealomas Arch Neurol and Psychiat 1931 XXV 937

55 GOLDHAMER K 1930 Normale Anatomie des Kopfes im Rontgenbild Thieme Leipzig 1930

56 GREENFIELD J G 1936 Some modern problems connected with the cerebrospinal fluid Edinburgh Med Jour 1936 XLIII 6[illegible]2

57 GUTTMANN L 1936 Roentgendiagnostik des Gehirns und Ruckenmarks durch Kontrastverfahren Springer Berlin 1936

58 HARE C C 1935 The cerebrospinal fluid obtained by lumbar and by ventricular puncture in tumor of the brain Bull Neurol Inst N Y 1935 IV

59 HEUER G J and DANDY W E 1916 Roentgenography in the localization of brain tumor based upon a series of one hundred consecutive cases Bull Johns Hopkins Hosp 1916 XXVII 311

60 HOLMES G 1919 The cortical localization of vision Brit Med Jour 1919 II 193

61 HOLMES G 1931 A contribution to the cortical representation of vision Brain 1931 LIV 4[illegible]0

6 HOLMES G and LISTER W T 1916 Disturbances of vision from cerebral lesions with special reference to the cortical representation of the macula Brain 1916 XXXIX 34

63 HORRAX G 19[illegible]4 Generalized external arachnoiditis simulating cerebellar tumor its surgical treatment and end results Arch Surg 19[illegible]4 IX 95

64 HORRAX G and BAILEY P 19[illegible]5 Tumors of the pineal body Arch Neurol and Psychiat 19[illegible]5 XIII 4[illegible]3

65 HORRAX G and PUTNAM T J 193[illegible] Distortions of the visual field in

of radiation in the treatment of cerebellar medulloblastomata — report of twenty cases Am Jour Roentgenol 1936 XXXV 429
28 DANDY W E 1918 Ventriculography following the injection of air into the cerebral ventricles Ann Surg 1918 LXVIII 5
29 DANDY W E 1919 Roentgenography of the brain after injection of air into the spinal canal Ann Surg 1919 LXX 397
30 DANDY W E 1933 Benign Tumors in the Third Ventricle of the Brain Diagnosis and Treatment Chas C Thomas Baltimore 1933
31 DANDY W E 1934 Benign Encapsulated Tumors in the Lateral Ventricles of the Brain Diagnosis and Treatment Williams and Wilkins Baltimore 1934
32 DANDY W E 1937 Carotid cavernous aneurysms (pulsating exophthalmos) Zentr f Neurochir 1937 II 77 and III 165
33 DAVID M and STUHL L 1933 Les meningiomes de la petite aile du Sphenoide Etude radiologique Jour de Radiol et d Electrol 1933 XVII 193
34 DAVIDOFF L M and DYKE C G 1935 Demonstration of normal cerebral structures by means of encephalography ventricles interventricular foramina and aqueduct of Sylvius Bull Neur Inst N Y 1935 IV 91
35 DAVIDOFF L M and DYKE C G 1937 The Normal Encephalogram Lea and Febiger Phila 1937
36 DAVIS L and CUSHING H 1925 Papillomas of choroid plexus Arch Neurol and Psychiat 1925 XIII 681
37 DEL RIO-HORTEGA P 1921 La glia de escasas radiaciones (oligodendroglia) Bol d l R Soc Esp d Hist Nat enero 1921
38 DOTT N M and BAILEY P 1925 Hypophyseal adenomata Brit Jour Surg 1925 XIII 314
39 DUFFY W C 1920 Hypophyseal duct tumors Ann Surg 1920 LXXII 537
40 DYKE C G 1930 Indirect signs of brain tumor as noted in routine roentgen examinations displacement of the pineal shadow Am Jour Roentgenol 1930 XXIII 598
41 DYKE C G 1936 The roentgen ray diagnosis of diseases of the skull and intracranial contents Chap 1 Diagnostic Roentgenology Ed R Golden Nelson N Y 1936
42 ELKINGTON J St C 1935 Metastatic tumours of the brain Proc Roy Soc Med 1935 XXVIII 1080
43 ELSBERG C A 1936 The sense of smell the localization of tumors of the frontal lobe of the brain by quantitative olfactory tests Bull Neur Inst N Y 1936 IV 535
44 ELVIDGE A R 1937 The cerebral vessels studied by angiography A Res Nerv and Ment Dis Proc 1937 XVIII
45 ELVIDGE A R PENFIELD W and CONE W V 1935 The gliomas of the central nervous system A study of 210 verified cases A Res Nerv and Ment Dis Proc 1935 XVI 107

84 NAFFZIGER H C 19 5 A method for the localization of brain tumors — the pineal shift Surg Gynec and Obstet 19 5 XL 481
85 NORTHINGTON P 1936 The hearing in patients with intracranial tumors Bull Neurol Inst N Y 1936 V 89
86 OLIVECRONA H and LYSHOLM E 19 Die chirurgische Behandlung der Gehirntumoren Springer Berlin 19
87 OLIVECRONA H 1934 Die Parasagittalen Meningeome Thieme Leipzig 1934
88 PARDEE I 193 Pituitary basophilism of Cushing — syndrome of the basophilic adenoma Bull Neurol Inst N Y 193 VI 185
89 PENFIELD W 19 3 Cranial and intracranial endotheliomata Hemicraniosis Surg Gynec and Obstet 19 XXXVI 65
90 PENFIELD W 19 3 Osteogenetic dural endothelioma true nature of hemicraniosis Jour Neurol and Psychopath 19 3 IV 2
91 PENFIELD W 19 4 Oligodendroglia and its relation to classical neuroglia Brain 19 4 XLVII 430
9 PENFIELD W 19 5 Cerebral pneumography its dangers and uses Arch Neurol and Psychiat 19 5 XIII 580
93 PENFIELD W 19 9 Notes on cerebral pressure atrophy A Res Nerv and Ment Dis Proc 19 9 VIII 346
94 PENFIELD W 19 9 Diencephalic autonomic epilepsy Arch Neurol and Psychiat 19 9 XXII 358
94a PENFIELD W 1931 Classification of Brain Tumours and its Practical Application Brit Med Jour 1931 I 33
95 PENFIELD W 193 Neuroglia normal and pathological Cytology and Cellular Pathology of the Nervous System vol II chapt IX 4 3 P Hoeber Inc New York 193
96 PENFIELD W 1932 Tumors of the sheaths of the nervous system Cytology and Cellular Pathology of the Nervous System vol III chapt XIX 954 P Hoeber Inc New York 19
97 PENFIELD W 1934 A contribution to the mechanism of intracranial pain A Res Nerv and Ment Dis Proc 1934 XV 399
98 PENFIELD W and BOLDREY E B 1937 Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation Brain 1937 LX 389
99 PENFIELD W and ELVIDGE A R 193 Hydrocephalus and the atrophy of cerebral compression Cytology and Cellular Pathology of the Nervous System vol III chapt XXVIII 1 01 P Hoeber Inc New York 193
100 PENFIELD W and GYLES H R 19 9 Cerebral calcification epilepsy Arch Neurol and Psychiat 19 9 XXI 1020
101 PENFIELD W EVANS J P and MACMILLAN J A 1935 Visual pathways in man with particular reference to macular representation Arch Neurol and Psychiat 1935 XXXIII 816
10 PENFIELD W and McNAUGHTON F 1938 Dural headache and the innervation of the dura mater — to appear shortly

ca cs of brain tumor The field defects and hallucinations produced by tumours of the occipital lobe Brain 1932 LV 499

66 HYLAND H H and BOTTERELL E H 1937 Frontal lobe tumours a clinical and physiological study Canad Med Assoc Jour 1937 XXXVII 530

67 KERSHMAN J 1938 Medulloblast and medulloblastoma a study of human embryos Arch Neurol and Psychiat — to appear shortly

68 KESCHNER M BENDER M B and STRAUSS I 1936 Mental symptoms in cases of tumor of the temporal lobe Arch Neurol and Psychiat 1936 XXXV 572

69 LAIDLAW G F 1930 Silver staining of the endoneurial fibers of the cerebrospinal nerves Am Jour Path 1930 VI 435

70 LINDAU A 1926 Studien uber Kleinhirncysten Bau Pathogenese und Beziehungen zur Angiomato is Retinae Acta Pathol et Microbiol Scand Supplementheft 1926 I 1

71 LYSHOLM E 1937 Das Ventrikulogramm Norstedt Stockholm 1937

72 MALLORY F B 1920 The type cell of the so called dural endothelioma Jour Med Res 1920 XLI 349

73 MALLORY F B 1925 Principles of Pathologic Histology Saunders Phila 1925

74 MASSON C 1931 Occurrence of calcification in gliomas Bull Neurol Inst N Y 1931 I 314

75 MERRITT H H and FREMONT-SMITH F The cerebrospinal fluid vol XI chapt XXXI Loose Leaf Medicine Nelson New York

76 MONIZ E 1931 Tumeurs cerebrales et l encephalographie arterielle Masson Paris 1931

77 MORTENSEN O A and WEED L H 1934 Absorption of isotonic fluids from subarachnoid space Am Jour Physiol 1934 CVIII 458

78 McCONNELL L H and CHILDE A F 1937 Pneumographic localization of tumors of the brain I Tumors of the lobes of the cerebrum Arch Neurol and Psychiat 1937 XXXVII 33

79 McCONNELL L H and CHILDE A F 1937 Pneumographic localization of tumors of the brain II Tumors involving the basal ganglia lateral ventricles brain stem and cerebellum Arch Neurol and Psychiat 1937 XXXVII 56

80 McLEAN A J 1936 Intracranial tumors Handb d Neurolog Bumke Foerster XIV 131 Berlin 1936

81 McLEAN A J 1936 Pituitary tumors Handb d Neurolog Bumke Foerster XIV 242 Berlin 1936

82 McQUARRIE I and PEELER D B 1931 The effects of sustained pituitary antidiuresis and forced water drinking in epileptic children Jour Clin Investig 1931 X 915

83 McNALLY W J FRICKSON T C SCOTT-MONCRIEFF R and REEVES D L 1937 Clinical observations on bone conduction Jour Laryng and Otol 1937 LII 295

84 NAFFZIGER H C 19 5 A method for the localization of brain tumors — the pineal shift Surg Gynec and Obstet 19 5 XL 481
85 NORTHINGTON I 1936 The hearing in patients with intracranial tumors Bull Neurol Inst N Y 1936 V 59
86 OLIVECRONA H and LYSHOLM F 19 7 Die chirurgische Behandlung der Gehirntumoren Springer Berlin 19 7
87 OLIVECRONA H 1934 Die Parasagittalen Meningeome Thieme Leipzig 1934
88 PARDEE I 1937 Pituitary basophilism of Cushing — syndrome of the basophilic adenoma Bull Neurol Inst N Y 1937 VI 183
89 PENFIELD W 1 3 Cranial and intracranial endotheliomata Hemicraniosis Surg Gynec and Obstet 19 3 XXXVI 657
90 PENFIELD W 19 3 Osteogenetic dural endothelioma true nature of hemicraniosis Jour Neurol and Psychopath 1 3 IV 7
91 PENFIELD W 19 4 Oligodendroglia and its relation to classical neuroglia Brain 1924 XLVII 430
9 PENFIELD W 19 5 Cerebral pneumography its dangers and uses, Arch Neurol and Psychiat 19 XIII 580
93 PENFIELD W 19) Notes on cerebral pressure atrophy A Res Nerv and Ment Dis Proc 1929 VIII 346
94 PENFIELD W 19) Diencephalic autonomic epilepsy Arch Neurol and Psychiat 1929 XXII 358
94a PENFIELD W 1931 Classification of Brain Tumours and its Practical Application Brit Med Jour 1931 I 337
95 PENFIELD W 193 Neuroglia normal and pathological Cytology and Cellular Pathology of the Nervous System vol II chapt IX 423 P Hoeber Inc New York 1932
96 PENFIELD W 193 Tumors of the sheath of the nervous system Cytology and Cellular Pathology of the Nervous System vol III chapt XIX 954 P Hoeber Inc New York 1932
97 PENFIELD W 1934 A contribution to the mechanism of intracranial pain A Res Nerv and Ment Dis Proc 1934 XV 399
98 PENFIELD W and BOLDREY E B 1937 Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation Brain 1937 LX 389
99 PENFIELD W and ELVIDGE A R 193 Hydrocephalus and the atrophy of cerebral compression Cytology and Cellular Pathology of the Nervous System vol III chapt XXVIII 1201 P Hoeber Inc New York 193
100 PENFIELD W and GEYELIN H R 1 9 Cerebral calcification epilepsy Arch Neurol and Psychiat 19 9 XXI 10 0
101 PENFIELD W EVANS J P and MACMILLAN J A 1935 Visual pathways in man with particular reference to macular representation Arch Neurol and Psychiat 1935 XXXIII 816
102 PENFIELD W and McNAUGHTON F 1938 Dural headache and the innervation of the dura mater — to appear shortly

cases of brain tumor The field defects and hallucinations produced by tumours of the occipital lobe Brain 1932 LV 499

66 HYLAND H H and BOTTERELL E H 1937 Frontal lobe tumours a clinical and physiological study Canad Med Assoc Jour 1937 XXXVII 530

67 KERSHMAN J 1938 Medulloblast and medulloblastoma a study of human embryos Arch Neurol and Psychiat — to appear shortly

68 KESCHNER M BENDER M B and STRAUSS I 1936 Mental symptoms in cases of tumor of the temporal lobe Arch Neurol and Psychiat 1936 XXXV 572

69 LAIDLAW G F 1930 Silver staining of the endoneurial fibers of the cerebrospinal nerves Am Jour Path 1930 VI 435

70 LINDAU A 1926 Studien uber Kleinhirncysten Bau Pathogenese und Beziehungen zur Angiomatosis Retinae Acta Pathol et Microbiol Scand Supplementheft 1926 I 1

71 LYSHOLM E 1937 Das Ventrikulogramm Norstedt Stockholm 1937

72 MALLORY F B 1920 The type cell of the so called dural endothelioma Jour Med Res 1920 XLI 349

73 MALLORY F B 1925 Principles of Pathologic Histology Saunders Phila 1925

74 MASSON C 1931 Occurrence of calcification in gliomas Bull Neurol Inst N Y 1931 I 314

75 MERRITT H H and FREMONT-SMITH F The cerebrospinal fluid vol VI chapt XXVI Loose Leaf Medicine Nelson New York

76 MONIZ E 1931 Tumeurs cerebrales et l encephalographie arterielle Masson Paris 1931

77 MORTENSEN O A and WEED L H 1934 Ab orption of i otonic fluids from subarachnoid space Am Jour Physiol 1934 CVIII 458

78 McCONNELL L H and CHILDE A F 1937 Pneumographic localization of tumors of the brain I Tumors of the lobes of the cerebrum Arch Neurol and Psychiat 1937 XXXVIII 33

79 McCONNELL L H and CHILDE A F 1937 Pneumographic localization of tumors of the brain II Tumors involving the basal ganglia lateral ventricles brain stem and cerebellum Arch Neurol and Psychiat 1937 XXXVIII 56

80 McLEAN A J 1936 Intracranial tumors Handb d Neurolog Bumke Foerster XIV 131 Berlin 1936

81 McLEAN A J 1936 Pituitary tumors Handb d Neurolog Bumke Foerster XIV 242 Berlin 1936

82 McQUARRIE I and PEELER D B 1931 The effects of sustained pituitary antidiuresis and forced water drinking in epileptic children Jour Clin Investig 1931 X 915

83 McNALLY W J ERICKSON T C SCOTT-MONCRIFFF R and REEVES D I 1937 Clinical observations on bone conduction Jour Laryng and Otol 1937 LII 295

tion seen in certain cases of le ion of the frontal lobe Brain 1933 LVI 40
t.4 WEED L H 1932 The meninges Cytology and Cellular Pathology of the Nervous Sy tem vol II chapt XIII 611 I Hoeber Inc N Y 193
1 5 WEED L H and McKIBBEN P S 1919 Pres ure changes in the cerebro spinal fluid following intravenous injection of solution of variou concentrations, Am Jour Physiol 1919 XLVIII 512
1 6 WEED L H and McKIBBEN P S 1919 Experimental alteration of brain bulk Am Jour Physiol 1919 XLVIII 31

Sept 1 1938

{

103 RLEVLS D L 1938 Clinical and experimental results with thorotrast Medicine — to appear shortly

104 RIDDOCH C 1935 Visual disorientation in homonymous half fields, Brain 1935 LVIII 376

105 ROUSSY G LHERMITTE J and CORNIL L 1924 Essai de classification des tumeurs cerebrales Ann d Anat path 1924 I 333

106 ROUSSY G OBERLING C and RAILEANU C 1931 Les neurospongiome Presse med 1931 XXXIX 977

107 RUSSELL C K and KERSHMAN J 1937 Spontaneous subarachnoid hæmorrhage and brain tumour Canad Med Assoc Jour 1937 XXXVI 568

108 SCHMIDT M D 1903 Ueber die pacchionischen Granulationen und ihre Verhaltnis zu den Sarkomen und Psammomen der Dura Mater Virchows Arch f path Anat 1903 CLXX 429

109 SCHUELLER A 1918 Roentgen Diagnosis of Diseases of the Head Mosby St Louis Mo 1918

110 SOSMAN M C 1927 Radiology as aid in diagnosis of skull and intracranial lesions Radiology 1927 IX 396

111 SOSMAN M C and PUTNAM T J 1925 Roentgenological aspects of brain tumors meningiomas Am Jour Roentgenol 1925 XIII 1

112 STEWART T G and HOLMES G 1904 Symptomatology of cerebellar tumours Brain 1904 XXVII 523

113 STRAUSS I and GLOBUS J H 1918 Spongioblastoma with unusually rapid growth following decompression Bull Neurol Inst N Y 1918 I 273

114 STRAUSS I and KESCHNER M 1935 Mental symptoms in cases of tumor of frontal lobe Arch Neurol and Psychiat 1935 XXXIII 986

115 STUCK R M and REEVES D L 1938 Some dangerous effects of thorotrast used intracranially with special reference to experimental production of hydrocephalus Arch Neurol and Psychiat — to appear shortly

116 THIEL R 1932 Rontgendiagnostik des Schadels bei Erkrankungen des Auges und seiner Nachbarorgane Springer Berlin 1932

117 TOOTH H H 1912 Some observations on the growth and survival period of intracranial tumours based on the record of 500 cases with special reference to the pathology of the gliomata Brain 1912 XXXV 61

118 TORKILDSEN A and PENFIELD W 1933 Ventriculographic interpretation Arch Neurol and Psychiat 1933 XXX 1011

119 TOWNE E B 1926 Erosion of the petrous bone by acoustic nerve tumor Arch Otolaryngl 1926 IV 515

120 VAN DESSEL A 1925 L incidence et le processus de calcification dans les gliomes du cerveau Arch Franco Belges de Chir 1925 XXVIII 845

121 VASTINE J H and KINNEY K K 1927 Pineal shadow as an aid in localization of brain tumors Am Jour Roentgenol 1927 XVII 320

122 VIRCHOW R 1860 Cellular Pathology Translation by Frank Chance Robt M de Witt New York I 1860

123 WALSHE F M R and ROBERTSON E G 1933 Observations upon the form and nature of the grasping movements and tonic innerva

CHAPTER VI A

MULTIPLE NEUROFIBROMATOSIS

By GORDON L. HEIN AND JAMES C REAVIS

Table of Contents

Definition — Multiple neurofibromatosis may best be considered as a member of a group of diseases the neuro ectodermal dysplasias It is a multiple neoplastic disease affecting ectodermal structures and the

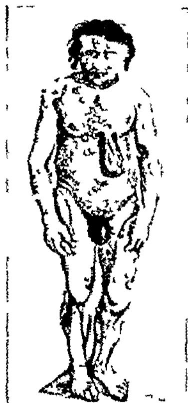


FIG 1 Tilesius patient From a drawing illustrating the monograph *Historia Pathologica Singularis Cutis Turpitudinis* (after Beattie and Dickson)

plexiform neuromas (the type which includes elephantiasis neuromatosa) He concluded that all these lesions arise from the connective tissue sheaths of peripheral nerves This opinion is expressed in the term neurofibroma which he applied to the entire group

Although abnormal pigmentations of the skin had been noted no special importance was attached to them until Pierre Marie in 1896 emphasized their frequent occurrence and diagnostic meaning[11] He dwelt also on the congenital and familial nature of the disorder Thibierge and Feindel in 1898 reported several patients with incomplete types or formes frustres of the disease who had no tumors of the skin

nervous system in particular, and because of the ubiquitous distribution of the latter, any organ of the body may become involved by new growths

Synonyms — The following terms are synonyms or refer to particular manifestations of the disease, von Recklinghausen's disease, molluscum fibrosum fibroma molluscum simplex, elephantiasis neuromatosa and pachydermatocele

The disorder derives its eponym from Friedrich Daniel von Recklinghausen (1833-1910) He was a pupil of Rudolf Virchow and later became professor of pathology at the University of Strasbourg where he remained for thirty years

History

The first known accurate delineation of the disease is the case report given by Tilesius in 1793[1] It was illustrated by a drawing which gave a clear picture of the peripheral form of generalized neurofibromatosis (Fig 1) Craigie in 1819 reported a similar case Barkow (1829) was one of the first to recognize the importance of differentiating patients with a solitary tumor from those suffering from the generalized disease[3 4] In 1840 Jacobovics added to the literature a description of two more persons affected with "molluscum"[5] In 1847 Virchow published the case history of a young man afflicted with the disorder whose grandfather, father and siblings had similar tumors[6] In 1849 Robert Smith conducted important pathological studies[7 8] He performed careful autopsies upon the bodies of two patients who had multiple neurofibromas He found no evidence of the proliferation of nerve tissue in the tumors but called the lesions 'neuromas' because of their intimate relation to nerve trunks The first report of malignant degeneration was given by Hitchcock in 186-, there were two other cases of multiple neuromas in his patient s family[9]

However it remained for von Recklinghausen to bring the disease to the attention of clinicians and pathologists throughout the world In 188- he presented in detail the autopsy findings of two cases[10] In both there were tumors of the skin and nerve trunks He examined the tumors microscopically noting that they were formed of bands and whorls of fibrous tissue and he demonstrated the presence of degenerating nerve fibrils within the substance of the tumors in some specimens He correlated the findings in neuromas of nerve trunks, neuromas of skin and

were convinced that these arose from aberrant embryonic nervous tissue and proposed a cell rest hypothesis This view was soon abandoned when it was shown by Antoni that degenerative type cells are sometimes present in the tumors and that these can be confused with nerve cells[2]

An interesting observation is that of Yakovlev and Guthrie[8] They note that the tumors are especially common on the cephalic and caudal ends of the body (scalp face back of the neck gluteal fold groin perineum and lumbosacral region) then on the shoulders armpits back and thighs They are exceptional on the hands and feet These authors point out that at a distance from the dorsal groove the tumors are less frequent suggesting that their origin (anlage) is related to the epiblast or the neural tube

Heredity — The *congenital and familial associations* of multiple neurofibromatosis are well known Typically there is at least some evidence of abnormal skin pigmentation present from birth This may be only a cafe au lait spot or a few small pigmented nevi More pronounced defects may be present from the beginning It is estimated that other members of a patient s family are involved in 15 to 20 per cent of cases[29, 30] It is probable for reasons to be presented later that this figure is too small

In 1918 Preiser and Davenport made a study of familial incidence in this disease[31] From the literature they collected a total of 43 cases Of these 138 were males and 105 were females They noted as had others before them that the disease tends to recur without a break in generations and is about as likely to have come from the patient s father or mother regardless of the sex of the patient The family histories of 119 males were examined The father was affected 49 times the mother 46 times and neither parent in the remaining 4 Of 79 females the father was affected in 29 the mother in 34 and neither parent in 10 Preiser and Davenport laid emphasis on the fact that abnormalities usually appear in a direct line of ancestry and thus suggest that the hereditary factor is a dominant one This factor (or gene) thus facilitates the production of nerve sheath tumors under conditions of appropriate stimulation

Breaks in generations actually or seemingly occur and present an apparent difficulty to the hypothesis that the factor is dominant However a patient s statement that his ancestors are not involved is obviously not always to be relied upon It often takes great pains on the part of the examiner to elicit the fact for example that the patient s father had a single pigmented spot on his thigh or abdomen Such a lesion may have escaped the patient s knowledge entirely Even when the ancestors show

or peripheral nerve trunks, but who had pigmented spots and moles[13, 14, 1] Mental and neurological defects accompanied the skin lesions Many other clinicians and pathologists have contributed to the recognition of multiple neurofibromatosis its widespread distribution throughout the body and its relation to other neuro-ectodermal dysplasias Their contributions will be cited in relation to subsequent portions of this chapter

Etiology

Predisposing Factors

The underlying defect in multiple neurofibromatosis is a developmental error of the neuro-ectoderm This much is accepted by all students of the disease There are, however, two major hypotheses as to the mode by which this defect is expressed Von Recklinghausen described the microscopic characteristics of the lesions and thought that they arose from nerve sheaths This concept was reiterated by Thomson in his monograph *On Neuroma and Neurofibromatosis* published in 1900[16] Penfield and Young still favor this hypothesis[17, 18, 19] Trotter maintains that there is a defect in the insulating system of the nerve fibers which leads to stimulation resulting in overgrowth of the surrounding structures be they fibrous tissue glia blood vessels etc, depending upon the region in which the insulation is defective[9]

In 1910 Verocay noted the arrangement of cells in parallel bands and nuclei in palisades in peripheral and central lesions of neurofibromatosis[1] He identified the cells of the central lesions with glial cells and those of the peripheral lesions with sheath of Schwann cells which he held to be peripheral glial cells" He concluded that the tumors might therefore be of glial or sheath of Schwann origin depending upon their site An objection to this view was the fact that the presence of collagen is easily demonstrated in neurofibromas and until rather recently it was thought that collagen can be produced only by fibroblasts Tissue culture studies by Nageotte and others however have shown that sheath of Schwann cells are capable of forming collagen and that these cells are of neuro ectodermal origin [3] They are peripheral glial cells Masson is the leading protagonist of this school and maintains that the disease is a generalized gliomatosis[4]

Lhermitte and Dumas[6] found cells in tumors of von Recklinghausen's disease which they thought were of central nervous system type They

that reported by Gardner and Frazier[1] They studied a family of five generations comprising a total of 217 members in which bilateral deafness was transmitted as a mendelian dominant character Thirty eight members were affected Autopsy was performed upon two members of the family and bilateral acoustic neurofibromas were found in both In this family there was no definite associated evidence of von Recklinghausen s disease It is cogent however that exactly similar tumors have been found in full blown cases of neurofibromatosis It appears that the manifestation of the defect was modified in this family by some concurrent constitutional factor which precluded expression in other parts of the body

Efforts on the part of modern French writers to unite multiple neurofibromatosis, tuberous sclerosis Lindau s disease and several other multiple tumor syndromes in the category of neuro ectodermal dysplasia have been successful in some respects[13, 14] There are clinical similarities and histological evidence to support the hypothesis of their close relationship[3, 14, 5, 16] In fact there are case reports of the simultaneous occurrence of at least portions of two or more of the syndromes in the same individual[1, 16, 4] However the heredofamilial evidence for their identity is extremely weak Each of the syndromes and especially multiple neurofibromatosis has a tendency to go its own way We have not found a report of the complete clinical syndrome of tuberous sclerosis (including adenoma sebaceum) in a von Recklinghausen family and reports of typical neurofibromatosis in a tuberous sclerosis family are rare[16] Tuberous sclerosis seems to be carried also as a mendelian dominant through several generations and achieves a varying degree of expression in different individuals of the same family but from an hereditary standpoint it must be considered as separate from von Recklinghausen s disease

Multiple neurofibromatosis is transmitted as a mendelian dominant character This implies that an individual heterozygous (bearing one gene) for the taint upon mating with an unaffected person will transmit the character to half his offspring who will display the defect This is shown by family studies as definitely as any hereditary trait is manifested in human beings No evidence for the existence of the character in homozygous form has yet been presented in multiple neurofibromatosis As a general rule once the taint is gone from a line of descent it is gone forever the possible exceptions occurring in the so called skipped generations It has never been known to reappear after its absence in two generations

no lesions on close examination, one or more may still have hidden tumors But accepting the condition that a generation is truly "slipped", the same phenomenon is known to occur in the course of transmission of so-called "dominant" traits in the lower animals, for example, polydactylism in fowls Preiser and Davenport concluded that "occasionally a dominant trait simply fails of expression in an individual who carries it" For an explanation of this phenomenon in the light of modern genetic concepts the reader is referred to Julian Huxley's *Evolution, the Modern Synthesis*[3] Huxley also points out that "dominance" in a mendelian sense is only relative These exceptions however do not detract from the rule and for practical purposes von Recklinghausen's disease is transmitted as a mendelian dominant

We may go even farther than this in the matter of inherited trends in the disease In some families the disorder is manifested in a similar manner in different individuals In the first place the location of the principal tumors may be the same In two brothers the left temple and left upper eyelid were involved[13] In another instance two half brothers had similar tumors on their right buttocks[31] Murray reported two children of seven and four years respectively who had similarly enlarged terminal phalanges A family observed by Czerny had a tendency in three generations to form huge tumors over the thoracic vertebrae[36] Numerous similar examples are on record

The behavior of the characteristic skin pigmentation also shows familial peculiarities Extensive pigmentation of a patient and her mother was noted by Herczel[3] Salomon reported similar coffee-colored flecks in brother and sister[38] Sutherland reported similar pigment spots in three generations[39] In certain families there are few or no pigment spots

A tendency to produce the rather uncommon confluent tumors (so called "elephantiasis") also runs in families Harbitz noted this in five generations[40]

Finally the significant and unfortunate tendency for the tumors to undergo sarcomatous change is especially marked in a few families Arnozan and Prioleau described sarcoma in two siblings[41] Genersich reported sarcomas in mother and son[31] In the family described by Hitchcock the growth of tumors accelerated during middle life throughout the family[9]

Thus it appears that the nature of the symptoms depends to some extent on a familial constitutional factor and that biotypes may be distinguished in this disease as in many others

Since the exhaustive review by Preiser and Davenport several very interesting family histories have been recorded The most remarkable is

not be undertaken except for definite symptomatic relief of an urgent nature[57]

Incidence

The disease has been described not only in persons of European extraction but also in Chinese Japanese Tamils Burmese and Negroes[58] A similar condition has been described in cattle horses dogs mules deer and even in certain fishes[16] [6]

The occurrence of abnormal skin pigmentation is common Many persons who are free from molluscа fibrosa or other nerve involvement show cafe au lait spots and multiple pigmented moles It is impossible in the present state of our knowledge to draw the line between these cases and formes frustres of the disease occurring in members of the families of those who have outspoken manifestations In an individual case of von Recklinghausen s disease the finding of pigmentary spots in other members of the family is taken as evidence of a heredofamilial taint but even in such an instance one may carry the pigmentary stigmata *all his life with no other abnormalities Fully developed neurofibroma* tosis is an uncommon disorder In a 19 year period at San Francisco City and County Hospital the final diagnosis included multiple neurofibro matosis in only sixteen patients an incidence of 0 006 per cent It is probable that some formes frustres without cutaneous tumors were missed On the other hand we cannot agree with Billow who calculates from the finding of eight cases in 500 persons he examined in a month that the incidence in the general population is as high as 1 6 per cent[61]

No authors since have collected such a large series as that reported by Preiser and Davenport in 1918[31] From their statistics they concluded that neurofibromatosis is a rare disease since only one out of 2 000 patients who go to skin clinics or dermatologists are afflicted with this disorder Such a survey has not been undertaken since but there is no reason to believe the result would be very different

On the other hand the incidence is much higher in institutions for the feeble minded and insane The association of neurofibromatosis with mental defect and occasionally with epilepsy is well known so it would be expected that a large number of victims of the disease would be found in these institutions Some patients with normal intellect are so grossly deformed that they seek shelter in such places to avoid contact with an *intolerant world Yakolev and Guthrie reported that a skin survey of* 500 male patients in the Monson State Hospital at Palmer, Massachusetts

Estimates given by most authors are that this disease is heredofamilial in only 15 to 20 per cent These figures are undoubtedly much too low and the principal reason for the error is the failure of the examiner to take a careful family history and to inspect other members of the family, nevertheless there are certainly patients whose parents and siblings have no stigmata Such cases suggest one of two possibilities, either that the same gene mutation occurs repeatedly, or that von Recklinghausen's disease is found in a purely phenotypic form in which the germ plasm is not tainted We incline toward the former view because in many family trees where the trait apparently arises de novo, it is subsequently transmitted in typical fashion It is a commonly known fact that the same gene-mutations arise spontaneously over and over again in such animals as *Drosophila*, and there is no reason to doubt that the same events occur in the human phylogeny as well

Exciting Factors

There is often a marked increase in the size and number of the tumors at puberty[50] This also is true during pregnancy[50, 1] Sutton described lesions which appeared during pregnancy , disappeared after delivery However, sometimes they remain[0, 51] It is felt that endocrine influences play a part in the development of the lesions but no particular endocrine organ or secretion has been implicated Associated endocrine disorders have been noted, but it is thought by most authors that they appear coincidentally or are at most an unusual expression of the same underlying defect Injury and exposure to cold have been mentioned as exciting factors for the development of skin tumors[30] Various infectious diseases have been noted to precede a marked increase in the size and number of the lesions, among these the most frequently mentioned are typhoid fever, diphtheria and pneumonia[53, 54, 5] The influence of these latter diseases is less well established, since the lesions in many cases increase suddenly for no apparent reason Whether or not repeated trauma or a single surgical excision can incite the growth of existing tumors is still in dispute About a century ago Sir James Paget made the observation that recurring fibroid tumors assume more and more malignant features the oftener they recur[6] Whether the surgeon's knife stimulates the growth of a pre-existing sarcoma or adds an irritant stimulus which converts a benign tumor to a malignant one is not known The impression nevertheless lingers that removal of these tumors should

fibers[17, 18, 19] It is thought by some pathologists that the two lesions may have an entirely different pathogenesis the former arising from the endoneurium and the latter from the perineurium [3, 61]

Multiple neurofibromas are found also on the deeper peripheral and visceral nerves These have the same microscopic appearance as the subcutaneous and pedunculated varieties but are prone to undergo sarcomatous change[4, 66] A special diffuse form of neurofibromatosis is known as *plexiform neuroma* or *elephantiasis neuromatosa* This is due to widespread overgrowth of the nerve sheath elements and separation of the nerve fibers Myxomatous degeneration is most common in these lesions Some cases of so called *familial hypertrophic neuritis*" are variations of plexiform neuroma in which the larger trunks are involved In both these conditions the microscopic anatomy is similar to that of the more discrete lesions[68]

As a general rule these tumors preserve their benign and encapsulated characteristics but occasionally either spontaneously or following surgical excision one of them begins to increase rapidly in size and to extend beyond its capsule This suggests sarcomatous change When such a change has occurred the microscopic appearance of the neurofibro sarcoma may vary from a fasciculated arrangement similar to that of an ordinary neurofibroma to a very anaplastic overgrowth of spindle shaped or round cells Very cellular growths present larger cells with little stroma Giant cells also occur The more rapidly growing tumors are composed of numerous small cells[4] The mode of spread of the peripheral sarcomas usually is by extension along the involved nerve trunk finally requiring amputation when local excision has repeatedly failed to arrest the growth of the neoplasm These tumors are not responsive to roentgen or radium therapy to any marked degree[68, 6] Tumors arising from the autonomic nerves occasionally undergo similar changes The outlook in all these cases of sarcomatous degeneration is bad and death while most often due to a process of direct extension may result also from rapidly growing blood borne metastases to the lungs[4] (see case 4)

A word should be said about the cafe au lait spots and pigmented moles which are so commonly a part of the syndrome It is rather disappointing that so little is seen microscopically in the cafe au lait spots The pigmentation usually is slight compared to that of the moles and is due to deposition of melanin in the basal layers of the epidermis[70] The moles are entirely similar to the common pigmented nevi which occur in almost everyone In neurofibromatosis they are usually present in

disclosed fifty-five patients who had cutaneous manifestations of neurofibromatosis[5] The skin lesions consisted of multiple skin polypi pigmented nevi and cafe au lait spots Four of these patients had epileptic seizures

When neurofibromatosis plays no apparent role in the patient's symptomatology, the skin lesions are often disregarded by the examiner It has been our experience that the brain may be explored for intracranial neoplasm of unknown type and the stigmata on the skin definite but not too obvious may be found only when carefully searched for postoperatively Many persons with a few small neurofibromas go entirely unobserved and suffer no symptoms which would bring them under medical care With this and the foregoing considerations in mind it can be seen that any estimate of the incidence of the disorder in the general population must be entirely nebulous when compared to symptom-producing diseases such as tuberculosis and heart disease

Pathology

Because of the extreme variation in the microscopic picture of the lesions it is impossible to give a composite description of a typical tumor This is emphasized by the fact that the pathological examination must often be correlated with the patient's clinical status before a proper interpretation can be given Not only do the lesions vary widely depending upon their location, but there are associated intracranial lesions which have a microscopic appearance entirely different from that of the peripheral masses[62] The situation is further complicated by a tendency for the lesions to undergo degeneration, both myxomatous and sarcomatous[63, 64, 6]

Peripheral Lesions

The common lesion *molluscum fibrosum (fibroma molluscum)*, is a soft tumor covered with skin Microscopically it has a reticulated or tangled appearance upon which may be superimposed a varying amount of cellular whorling or palisading With special stains neurofibrils sometimes may be seen passing through the tumor tissue The tumors of multiple neurofibromatosis according to Penfield and Young differ from solitary perineural fibroblastomas (neurinomas or schwannomas) in that the latter show marked palisading of nuclei and contain no nerve

hyaline degeneration forming small pearls If these subsequently calcify they are known as *psammoma bodies* or '*brain sand* When the tumors are growing rapidly, the cells are less well differentiated Multiple meningiomas have been noted often enough in generalized neurofibromatosis to be considered a definite part of the syndrome in spite of differences of opinion regarding their cellular pathogenesis (See also Penfield and McLachern s section on Meningeal Fibroblastomas Vol VI Chapt XI of Oxford Medicine)

Lesions similar to if not identical with those of tuberous sclerosis are found also in von Recklinghausen s disease These are hard plaques of glial overgrowth occurring in the cerebrum brain stem cerebellum *and spinal cord While some authors maintain that the lesions in the* two diseases can be differentiated microscopically the majority agree with Bielschowsky who felt that the process involved in both is a diffuse gliomatosis which may involve the spinal cord as well as the brain[6] The glial elements develop defectively from the primitive glial cells or spongioblasts, thus accounting for those cases in which glioblastomas also occur These glial cells sometimes attain an enormous size Along with this gliosis there may be a vascular hyperplasia and the formation of hemangiomas Cystic cavities sometimes form leading to symptoms resembling those of syringomyelia when they involve the medulla or spinal cord It is postulated by some authors that changes of the same type occurring in the eye cerebellum and intraabdominal organs may be the basis of *von Hippel* and *Lindau s syndromes*[7] Certainly in those cases in which gliotic and cystic lesions are present in the brain liver and kidneys it is impossible to separate the changes of von Recklinghausen s disease from those of these other neuro-ectodermal dysplasias (*see K family individual O K*)

Spongioblastoma polare is a glioma of the brain which sometimes complicates multiple neurofibromatosis[64] This is a tumor which involves the optic chiasm or brain stem usually in children but is found also in the brain stem or corpus callosum in adults with von Recklinghausen s disease It is a slowly growing tumor which sometimes is extremely sensitive to roentgen radiation It is usually inoperable when discovered because of the vital structures it involves Because of its microscopic appearance it has been called a '*central neurinoma*' The elongated cells arranged in long rows bear a superficial resemblance to those of an acoustic neurinoma Silver impregnation shows long unipolar or bipolar processes which characterize the cells as spongioblasts These tumors may undergo cystic degeneration

greater numbers Of interest in this regard is Masson's view that all nevi are of neural origin and are proliferations of the entire end apparatus of the sensory nerves of the skin[71]

Central Lesions

Several types of intracranial lesions are observed The most common are acoustic neurofibromas *(neurinomas)* and multiple meningiomas *(meningeal fibroblastomas* or *endotheliomas)* The former occur in the cerebellopontine angle and grow from the sheath of the acoustic nerve They are firm encapsulated tumors which displace the brain stem and other nearby structures Some authors consider them to be fibroblastomas, but Masson believes they arise from glial elements They are similar in structure to the solitary neuromas *(perineural fibroblastomas)* of other cranial and peripheral nerves and to those of spinal nerve roots (*"hour-glass"* or *"dumb-bell" tumors)*[73] Microscopic examination shows elongated nuclei arranged in whorls and palisades Cell outlines are vague with a fibrous or collagenous background In some cases neurofibrils may be demonstrated passing through the tumors but usually they are absent There is almost always an elevated cerebrospinal fluid protein with these tumors (see also Penfield and McEachern's section on Cerebellopontile Angle Tumors and on Perineural Fibroblastoma in Vol VI Chapter VI of Oxford Medicine)

Meningiomas are common intracranial neoplasms occurring singly When they are a part of von Recklinghausen's disease, they are usually multiple and not uncommonly associated with acoustic neurofibromas *(Wishart's disease)*[74] They often occur in great numbers in this condition sometimes involving the spinal meninges as well As is the case with the solitary lesion, they most often arise near the superior longitudinal sinus but may grow from any portion of the dura They arise from arachnoid villi and pacchionian bodies but also are found in regions where these structures are absent Penfield regards them as meningeal fibroblastomas[17] These tumors press on the brain, forming a deep bed from which they may be easily enucleated at autopsy, but during life they are quite vascular and are supplied by large vessels from the overlying bone They are adherent to the dura and do not penetrate the brain but the overlying bone is often invaded Meningiomas often calcify They then present a characteristic or even pathognomonic x ray picture from which the diagnosis is made Microscopically these tumors consist of elongated cells arranged in whorls The whorls may undergo

simultaneous presence of neoplasms Spina bifida is a common skeletal defect in generalized neurofibromatosis All these lesions may be classed as congenital abnormalities whose relation to von Recklinghausen's disease is established but whose pathogenesis at present is obscure

Welch, Ettinger and Hecht[79] recently have called attention to another spinal lesion sometimes confused with hour glass neurofibroma This is the intrathoracic meningocele which protrudes in the thorax in the region of the pedicles Of eight patients described five have had definite cutaneous neurofibromatosis Our own patient[79b] in conformity to the usual findings had no signs of cord compression although a large mass presented in the thorax Several vertebral pedicles were entirely destroyed some vertebral bodies were eroded and a marked kyphoscoliosis was present The diagnosis was established by myelography and intraspinal air contrast studies Operations on intrathoracic meningoceles have been accompanied by fatality in most cases and such operations probably should be avoided at least until better surgical methods have been devised

Neurofibromas of the periosteal nerves may cause irregularities in the contour of bones may extend outward in pedunculated fashion or may erode inward through the cortex[53] They are pathologically identical with the other peripheral nerve sheath tumors The femur is affected most often in this manner

There are however entirely different bone lesions which do not arise in the periosteum rather they *occur in the medullary region and* produce single or multiple cystic lesions of one or a few bones[78 79 80] Histologically these lesions have a fibrous or myxomatous structure with no great similarity to neurofibromas In a recent article Thannhauser has described these defects in full blown cases of neurofibromatosis and in other cases having cafe au lait spots and other pigmentary changes but no peripheral neurofibromas[81] He endeavors to prove that these lesions are due to degenerated intramedullary neurofibromas In reviewing the six original cases described by von Recklinghausen as osteitis fibrosa cystica' he points out that only two were definitely of the type attributable to hyperparathyroidism and that the rest show more or less local cyst formation Thus he links multiple neurofibromatosis of von Recklinghausen and von Recklinghausen's disease of bone These lesions are generally classed under the heading of fibrous dysplasia of bone The changes are localized and are not associated with the diffuse rarefaction of bone which accompanies hyperparathyroid bone cysts The relation of these lesions to Albright's syndrome is not known

Skeletal Lesions

Skeletal abnormalities are of several types [6, 77, 78, 9] In general they may be divided into deformities of unknown pathogenesis, neurofibromas of the periosteal nerves and cystic or neoplastic changes inside the bones

The most common in the first group are spinal torsions of the scoliosis and kyphosis types In some of these cases the vertebrae are displaced upon one another by neurofibromas of the nerve roots Usually however, such specific lesions are absent Deformities of the thoracic cage, such as funnel chest, belong in this category Of similar unknown causation is the diffuse overgrowth of an extremity or digit called "local gigantism" (Fig 2)[77] This usually is present from birth or infancy but the affected member continues to outgrow the rest of the body The overgrowth affects bones and soft tissues in like fashion so that often the outside member would be normal in all respects if it belonged to a giant That local gigantism is due to neurotrophic influences is suspected but unproved [8] In some cases of elephantiasis of an extremity the bones are diffusely enlarged but an extremity may be enlarged without the



Fig 2 Local gigantism X ray examination showed the bones of the toe to be enlarged in proportion to the soft tissues

Recklinghausen in his original monograph[10] but were dwelt upon at length by Marie and Chauffard[11, 12, 13] Ordinarily they accompany cutaneous or subcutaneous tumors French clinicians coined the term *formes frustres* to cover the situation in which they exist alone or with mental or neurological abnormalities implying that the development of the full syndrome is incomplete The spots vary upward in size from a diameter of 1 or 2 centimeters Their color is tan or brownish resem-



Fig 3 Pedunculated molluscoid lesions Note the scattered small dark nevi which are almost confluent in some areas This man is partially paralyzed on the left side and has a speech defect

bling coffee with milk or cream The shade may be uniform or variable The margins are quite sharply demarcated and are ovoid or somewhat irregular There is nothing unusual to be felt for the texture of the skin is normal and the lesions are not raised unless the area is further involved by mollusca or other tumors Common locations are the gluteal region the thorax the upper arms and the thighs They occur also on the neck

Endocrine Abnormalities

The endocrine organs especially the pituitary and adrenal glands, have been sites of neurofibroma formation These lesions do not differ from those found elsewhere but may lead to deficiency in the secretions of these glands Carcinomas of the adrenals and pheochromocytomas have been described[91] These are possibly a part of the generalized disease, or they may be incidental lesions related to some other congenital abnormality Diabetes occurring with von Recklinghausen's disease has been reported[9] Neurofibromas in the thyroid gland have not been proved to be a cause of hypothyroidism, although these tumors have been found in persons with hypothyroidism and in cretins[86] Endocrine abnormalities, principally of the pituitary varieties including acromegaly, Lorraine-Moon-Biedl syndrome and Frohlich's syndrome, have been described accompanying multiple neurofibromatosis[86, 8] It is questionable whether there is any direct etiological relationship between them except for the possibility that both may be due to coexisting underlying congenital abnormalities Certainly these coincidental conditions are seen rarely, although their occurrence is not surprising since it is a frequent observation that congenital defects of all sorts usually are multiple

Miscellaneous Lesions

Smooth-walled cysts of the renal cortex and of the liver have been encountered Their histogenetic origin has not been clarified Gliotic patches in the retina have been found and have led to the coining of the term *phakomatoses* to include *tuberous sclerosis* and *von Hippel Lindau's* disease in which similar lesions are present sometimes[88, 89] It is impractical to give a complete account of the organs which have been found involved in generalized neurofibromatosis but as a final note of emphasis upon the ubiquity of distribution of the lesions it may be noted that the stomach intestines mesentery ovaries and urinary bladder in addition to the other organs mentioned above, have all been the sites of tumor formation[90, 91, 92]

SYMPTOMS AND DIAGNOSIS

Cutaneous Pigmentation

Cafe au lait spots (Figs 4 7 and 8) are one of the striking diagnostic signs of neurofibromatosis They were described rather vaguely by von

neuro ectodermal dysplasia which may be manifested in the same individual[93]

Aside from the café au lait spots and discrete pigmented nevi there is a less well known variety of pigmentary abnormality which was described by Marie[11] This he designated as a *small seed bed of brownish dots* (*semis de points brunâtres*) (Fig 4) It is composed of numerous small brownish freckle sized flat nevi set close together in a patch which varies from 1 to 5 centimeters in diameter Sometimes there is a background of lesser pigmentation resembling a cafe au lait spot This

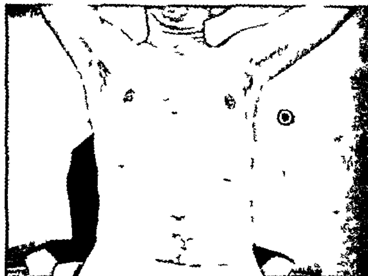


Fig 5 Mollusca fibrosa in the nipple region In this location they take on the deep pigmentation of the areola

lesion we have found to be even more characteristic of neurofibromatosis than the ordinary cafe au lait spot We have encountered it only in overt cases or in members of a family in which frank von Recklinghausen s disease is present while we have seen cafe au lait spots in persons who are otherwise normal and of normal family background

Peripheral Tumors

Neurofibromas of the skin are known as *mollusca fibrosa* (or *fibromata mollusca*) Their color usually is that of the surrounding skin but

and abdomen Less frequently the face is involved but to our knowledge the palms and soles always escape

The *common nevi* are of the small, flat, deeply pigmented variety These are often scattered over the whole trunk and the extremities in great profusion (Fig 3) They do not differ individually from those seen upon the skin of almost every normal person Small vascular nevi



Fig 4 Seed bed pigmentary lesion described by Pierre Marie In this case the small flat nevi over lie a cafe au lait spot The lesion was on the outer aspect of the left thigh

have been described also An unusual lesion is the "*nevus anemicus*" of Vorner[93] This is a small avascular area demonstrated more clearly when the surrounding skin is made hyperemic by gentle rubbing It is not a true mole or nevus but an area in which the capillaries are constricted while those of the surrounding skin are dilated Port wine stain *(nevus flammeus)* and *adenoma sebaceum* have been reported rarely in patients having neurofibromatosis but are more characteristic of other types of

of nerve sheath involvement so that all gradations are observed The sites of predilection for plexiform neuromas are the forehead neck anterior thorax and abdominal walls The lower extremities are involved also causing a condition known as *elephantiasis neuromatosa* Plexiform neuromas of other portions of the body including the ear lobe have been described

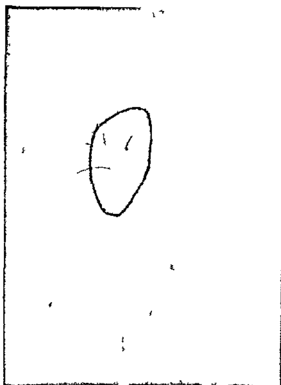


Fig 6 A molluscum fibrosum in an early stage of development it is encircled by a line A few coarse hairs arise from the surface of the lesion

Certain points are to be noted in regard to these tumors The superficial ones sometimes undergo myxomatous degeneration ulcerate and exude noisome sebaceous material Rarely do they become secondarily infected and discharge purulent material[1] In a very few cases patients have noted that changes in the weather are accompanied by congestion and itching of the skin tumors[1] While the molluscoid tumors do not

they may have a bluish cast because of pressure atrophy of the corium When they occur in the nipple region, they take on the pigmentation of the areola (Fig 5) Sometimes they are found within a café au lait spot, or they may be coffee-colored in themselves Some are speckled with small, brownish nevi Usually they are free from coarse hairs, but occasionally a few coarse hairs are present upon some of the flatter ones, and the lesions are similar in appearance to nonpigmented, hairy moles (Fig 6) They vary in size, shape, number and distribution in the individual case but have the common characteristic of being soft and velvety to the touch Their texture has been described as that of a scrotum without testes In size they range from a few millimeters up to the dimensions of a hen's egg or larger In general the tumors are raised or pedunculated They are usually not tender or painful but sometimes tender nodules *(tubercula dolorosa)* are found in the region of the joints or on the face or breasts They vary in number from a very few to thousands, of different sizes and shapes The regions most often affected are the thorax abdomen, neck and face The extremities are involved less often and the palms and soles very rarely In those exceptional cases where the latter are affected, the lesions are flat and indurated with the appearance of callosities

As a general rule, the sessile and pedunculated skin tumors follow no special nerve trunk distribution but in many cases there are deeper tumors lying along the course of nerve trunks Those most often involved are the nerves of the upper extremities and the intercostal trunks The lesions are fusiform or nodular and vary up to several centimeters in diameter They should always be felt for because sometimes they are too deep to be visible Some very large ones are occasionally found *(tumeurs royales)* They are firmly attached to the nerves usually symmetrically disposed about their circumference They are firm and easily movable Fixation suggests malignant degeneration and invasion of surrounding structures In most cases they cause no pain and are not tender There may be only a few nodules, or the entire course of a nerve may be involved in all its branches In some cases of von Recklinghausen s disease they are the only apparent tumors, but more often they are accompanied by the molluscoid skin lesions

Plexiform neuromas (pachydermatoceles) (Fig 7) are larger pendulous masses or even wide aprons of neurofibromatous skin and subcutaneous tissue Their surfaces are soft and irregular sometimes indented with dimples or raised by separate conglomerate tumors The essential difference between these and the smaller lesions is only in the confluence

the disease any type of pressure symptom may arise when the cranial and spinal cavities are the sites of lesions. Acoustic neurofibromas cause dizziness deafness and tinnitus. As the tumors grow the nearby cranial nerves and the cerebellum are encroached upon. Similar tumors have been found to involve all the cranial nerves. Meningiomas are an integral part of the syndrome of diffuse central neurofibromatosis. Both of these tumors may lead to signs of increased intracranial pressure. Neurofibromas and meningiomas of the cord produce the signs of extramedullary tumors and by nerve root involvement especially in the so called hour glass or dumb bell lesions are prone to cause intractable pain. In the presence of cafe au lait spots or skin tumors no neurological abnormalities however slight can be safely disregarded. We emphasize *this because of the easy operability of many of the lesions and the marked* relief which may be given by early surgery. This is often true even when the lesions are multiple. If let alone they may cause irreparable central nervous system damage. The dangers of malignant recurrence are far outweighed by these considerations in intracranial and intraspinal lesions.

Many persons afflicted with neurofibromatosis are mentally normal. There is however, an unquestionably high incidence of intellectual defect in the disorder[31]. Epileptiform seizures and upper motor neurone pareses have been noted in certain cases[5]. These defects often can be correlated with autopsy findings of gliotic patches throughout the brain especially in the cerebral cortex. These lesions are similar to those of tuberous sclerosis and possibly identical with them.

Besides the above mentioned neoplasms which are not unusual gliomas especially *spongioblastoma polare* in rare cases involve the optic chiasm optic nerve trunks brainstem and cerebellum (see family K individual Dor K.). They behave in a manner similar to the isolated lesions and are usually found in young persons. The occurrence of signs of rapidly increasing intracranial pressure in a young person with stigmata of neurofibromatosis would immediately suggest the presence of such a lesion. Diffuse involvement of the cauda equina has been reported. This condition leads to bladder paralysis and distention and severe perineal pain with loss of sensation in the perineal and sacral regions.

A few cases of retinal tumors have been described[9, 24]. They were single or multiple grayish glial neoplasms. In one case the pathological diagnosis was neuroma of the nerve head. The others were similar to the gliotic retinal lesions of tuberous sclerosis. Such tumors might call attention to their presence by interfering with vision or by causing a gray reflex on gross physical examination. They must be very rare.

undergo sarcomatous change those lying along the nerve trunks may do so Small tumors are usually benign, but the larger masses over 5 centimeters in diameter especially if they are growing rapidly, should arouse suspicion of neurofibrosarcoma resulting from malignant degeneration

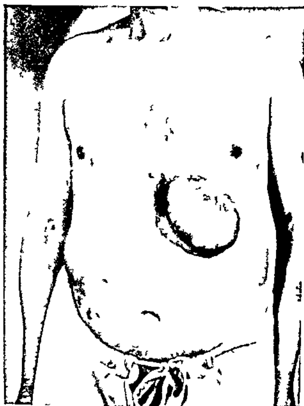


Fig 7 Plexiform neuroma Cafe au lait spots small flat nevi and several mollusca fibrosa are also shown

Nervous System Changes

The most common signs and symptoms of neurofibromatosis, aside from the skin lesions are caused by involvement of the nervous system both peripheral and central Tumors of the peripheral nerve trunks sometimes cause pain muscular atrophy or paresis in the region of distribution of the affected nerves Because of the ubiquitous nature of

In addition to the lesions mentioned above, it should be borne in mind that any organ may be expected to be the site of nerve tumor involvement A case in which hepatomegaly and splenomegaly were present is on record[31]

Endocrine Abnormalities

Since endocrine abnormalities are not a frequent accompaniment of the disease and are not necessarily a part of it their diagnostic importance is small Their presence in a patient having typical skin lesions should however lead to a search for the cause of the endocrine abnormalities In some cases a neurofibroma encroaching on an endocrine gland may be removable

Bone Changes

A careful examination for skeletal defects should always be made Kyphosis and scoliosis are the most common We have noted their presence in about 25 per cent of the patients we have studied Funnel-chest is a lesion which belongs in the same group Another defect frequently reported is that of local gigantism This is usually confined to a finger or toe (Fig 2) but a whole extremity may be involved This condition is not to be confused with elephantiasis which is due to neoplastic soft tissue infiltration and may cause great deformity of an extremity In local gigantism the bones and soft tissues are normal except for an increase in size The long bones and pelvis may be involved by neurofibromas arising in the periosteum causing firm masses attached to the bones Cystic lesions in the medullary portion of bones may occur singly or in great numbers in one or more bones especially in the femurs These have been discovered by x ray examination but in some cases they are noted only after pathological fractures have occurred[9] These lesions sometimes cause an increase in the length of bones (see also Grollman s section on Neurofibromatosis Vol IV Chapt XVI of Oxford Medicine)

Summary

A case of von Recklinghausen s disease when the patient is covered with cafe au lait spots pigmented moles and soft tumors of varying sizes

Visceral Involvement

Neurofibromas as a part of the generalized disease are found in the thorax, arising usually from the intercostal nerves The pleurae are often involved by these lesions The phrenic, vagus and sympathetic trunks also have been the sites of tumors The tumors may obstruct air passages the esophagus and the great vessels The heart and pericardium are seldom involved The lung parenchyma is not affected by neurofibromas but it is the most frequent site of blood borne metastases from neuro fibrosarcomas[6] Chest films should always be obtained when malignant degeneration of a tumor is suspected

Neurofibromas have been found in the nasopharynx (see family 'K', individual 'O K ') Although the mouth and mucous membranes are seldom involved by tumors an unexplained *macroglossia* sometimes occurs This is similar to local gigantism of an extremity or digit and the enlargement is not due to neoplastic tissue Neurofibromas of the tongue have been reported, however

Single and multiple neurofibromas of the stomach have been re ported These may simulate gastric ulcer or carcinoma by producing dyspepsia and bleeding Neurofibromas of the small intestine have been noted but they usually are discovered only at autopsy, as are those of the mesentery and do not produce symptoms of obstruction They are more common in the rectum where they may ulcerate and bleed Mega colon is sometimes associated with the bowel tumors Multiple smooth walled cysts of the liver have been found at autopsy without however having caused any signs of their presence during life

Neurofibromas of the bladder have been a source of hematuria On cystoscopic examination they have a smooth whitish appearance Removal of these tumors, which are usually multiple, generally is followed by recurrence with eventual blockage of the ureters Multiple cysts of the renal cortex may occur, similar to those of the liver The histogenesis of these lesions is not known but they have been a cause of hematuria Adenocarcinoma of the kidney has been found in a few patients but its relation to the generalized disease is uncertain Lesions of the male genital organs include neurofibromas of the testis scrotum and penis In women ovarian uterine vulval and labial lesions have been noted The large retroperitoneal autonomic, nerve plexuses frequently have been the site of neurofibromas and these lesions have the dangerous tendency to undergo sarcomatous change Large tumors displace the abdominal viscera and this displacement may be the only clue to their presence

Café au lait spots and small neurofibromas were also present The large tumor had been present since childhood and had grown slowly but steadily A few small tumors appeared at puberty but had never been very numerous He had no complaints referable to neurofibromatosis except the inconvenience of the large tumor This mass was removed by wide surgical excision at the insistence of the patient

Not all victims of the disease are so fortunate The following patient had widespread central nervous system changes with only moderate skin involvement

Case 2 (Fig 3) A 30-year old white man had *weakness of the legs for* 4 years and an increasing tendency to drag the left leg His mother was debilitated by a disease diagnosed as multiple sclerosis He had numerous cafe au lait spots small nevi and mollusca on the trunk and extremities The mullusca had increased in number at puberty A large seed bed *lesion (Fig 4) was noted on the left leg Weakness of the left arm and leg* were marked His speech was tremulous and hesitant but his mentality was not impaired Neurological examination revealed hypesthesia on the ulnar aspect of the left hand increased muscle tone in the left arm and leg and increased tendon reflexes on the left The abdominal and cremasteric *reflexes were absent The Babinski and Hoffman signs were positive bilaterally* Bilateral ankle clonus was present The spinal fluid pressure was normal Some observers thought that the neurological abnormalities were due to multiple sclerosis Our diagnosis was central and peripheral neurofibromatosis A year later the left hemiparesis had increased and the patient had *developed an ulcerative cystitis The possibility of cauda equina involvement* was entertained but not proved

The extent of skin involvement does not necessarily parallel the degree of central nervous system involvement This is well demonstrated by the next case report

Case 3 A 32 year old white man presented himself for study because of headaches and epileptiform seizures during the previous 6 months He had one small cafe au lait spot two small neurofibromas of the scalp and a few small mollusca on the trunk and extremities These lesions were so insignificant in appearance that the diagnosis of neurofibromatosis was not entertained before craniotomy The patient s mother and sister each had one cafe au lait spot but no skin tumors The patient was euphoric in spite of *his headaches Reflexes were more active on the right Left facial* weakness was present The right optic disc showed minimal papilledema The spinal *fluid* pressure was 90 millimeters X ray studies including ventriculography demonstrated a space-consuming lesion in the right frontal region

is one of the most obvious diagnoses in medicine, but the formes frustres are more difficult to evaluate Not everyone who bears pigmentary patches or moles is affected with the taint, but when these stigmata occur either alone or with mental and neurological symptoms the disease must be suspected Occurring in an otherwise unaffected member of a marked family they are as diagnostic of the mutilated gene as are the tumors themselves Sometimes the pigmentary changes occur with skeletal abnormalities such as kyphosis or local gigantism of an extremity or digit Such a combination of signs should leave no doubt It is our opinion that the "seed-bed" lesion of Pierre Marie is an absolutely pathognomonic stigma of hereditary contamination So far as we know, it has never been seen except in those with the disease or the hereditary background Persons bearing this lesion transmit the disease as though they had the full-blown manifestations

Course with Case Reports

In an heredofamilial disease the course of the illness must be considered not only from the standpoint of the individual but also from that of the family Undoubtedly there are many whose only symptom of the disease is the skin lesion These persons would not be likely to consult a physician for this condition and the disease would be seen in them only incidental to some other disorder For this reason the reports in the literature are greatly weighted in favor of the more serious forms of neurofibromatosis

In the ordinary instance the patient lives to old age unless attacked by a more serious illness Puberty and pregnancy often cause an increase in the size and number of the skin tumors but this may still cause no great inconvenience because the tumors usually occur on the surfaces of the body which are covered by clothing Occasionally however, a person will request surgical removal of a tumor for cosmetic reasons or because it is located in an inconvenient place

Illustrative Cases

Case 1 (Fig 7) A 49-year old white man sought medical advice because of a plexiform neuroma on the left lower anterior thorax and because of angina pectoris No other members of his family were affected

tissues of the injured region In April 1942 the left leg was amputated through the lower third of the thigh Pathological examination at the time of operation showed the lesion to be a neurofibrosarcoma X ray examination soon after surgery showed metastases to the lungs The patient died two months after operation

The relation of trauma to sarcomatous change is not usually so clear as it seems to be in this instance This case is also atypical in that the tumor which developed was of a high grade of malignancy and metastasized to the lungs very early The lesions in the lungs were undoubtedly present at the time of operation Neurofibrosarcomas are usually of low grade malignancy spread by local extension and metastasize by way of the blood stream either late or not at all

The following family tree of four generations exemplifies the mode of transmission of the disease and illustrates some of the complications which are seen occasionally

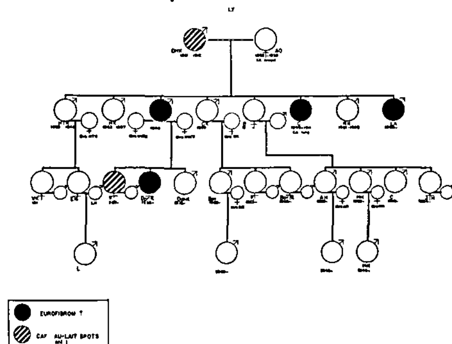


Fig 9 Family K The figure indicates the individual who showed neurofibromata and cafe au lait spots

Electroencephalography showed an abnormal focus in this area Craniotomy was performed disclosing at least 5 meningiomas in the right parasagittal frontal and parietal cortical areas One tumor 4 centimeters in diameter was removed The headaches were relieved and the neurological findings improved after surgery There were no convulsions in the three months period during which the patient was observed Several meningiomas remain and relief is only temporary



Fig 8 Neurofibrosarcoma in von Recklinghausen's disease Note the cafe au lait spots and mollusca fibrosa on the buttock

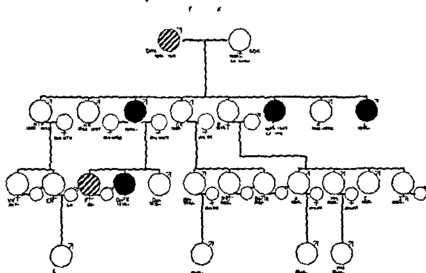
The next case report is presented as an example of the sarcomatous lesions which sometimes develop in patients with neurofibromatosis

Case 4 (Fig 8) A 49-year old white man had a rapidly growing tumor of the left calf He had numerous cafe au lait spots, present from infancy, and multiple nodular mollusca which had been present for twenty years or more on the arms abdomen chest back and legs No similar lesions were known in other members of his family Early in 1941 he sustained a heavy blow to his left calf Soon afterward a tumor began to grow in the deep

tissues of the injured region In April 194 the left leg was amputated through the lower third of the thigh Pathological examination at the time of operation showed the lesion to be a neurofibrosarcoma X ray examination soon after surgery showed metastases to the lungs The patient died two months after operation

The relation of trauma to sarcomatous change is not usually so clear as it seems to be in this instance This case is also atypical in that the tumor which developed was of a high grade of malignancy and metastasized to the lungs very early The lesions in the lungs were undoubtedly present at the time of operation Neurofibrosarcomas are usually of low grade malignancy spread by local extension and metastasize by way of the blood stream either late or not at all.

The following family tree of four generations exemplifies the mode of transmission of the disease and illustrates some of the complications which are seen occasionally



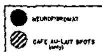


Fig 9 Family K The figure indicates the individuals who showed neurofibromata and cafe au lait spots

D H K had cafe au lait spots on the trunk which were called grease spots by members of the family He had no known tumors At the age of 50 he died suddenly from a massive upper gastrointestinal hemorrhage His health was said to be perfect up to that time

W K a 6[illegible] year old man had numerous typical cafe au lait spots and soft elevated molluscoid tumors One tumor the size of a lemon protruded from the left costal margin He complained of epigastric pain relieved by food of weight loss and of constant pain in the left costovertebral angle Carcinoma of the stomach was suspected but not proved by extensive x ray studies He had some diminution of hearing in the left ear but this was not due to nerve involvement

O K brother of W K had local gigantism of second left toe and cafe au lait spots from infancy In 1924 he had symptoms of a cerebellar tumor A posterior decompression was performed at that time but no tissue was removed X ray therapy was given following operation The patient showed marked improvement and led a practically normal life for 3 years He was seen in April 1947 for pain in the left thorax and arm He had numerous molluscoid skin lesions and cafe au lait spots A tumor was seen in the right fossa of Rosenmuller and on excision proved to be a neurofibroma X ray examination showed a large mass in the apex of the left chest Surgical removal of this mass was attempted but was unsuccessful because of the involvement of mediastinal structures Pathological examination showed the tumor to be a carcinoma rather than a neurofibrosarcoma as was expected The patient died August 1947 at the age of 48 Autopsy confirmed the surgical diagnosis of carcinoma of the lung and metastases were found in the brain and adrenals Gliotic patches in the brain similar to those found in tuberous sclerosis were present There was a 3 × 3 × 1 centimeter cyst in the left cerebellar hemisphere and there were smaller cysts in the optic radiation in the cortex of both kidneys and in the liver which raised the question of Lindau s syndrome although no angioma was found in the wall of the cerebellar cyst The patient also had a basal cell carcinoma of the skin overlying the sternum

L K a 42-year old man had cafe au lait spots A single plexiform neuroma arose from the forehead and left upper eyelid This tumor had occluded the vision of the left eye since childhood so that there was no vision in the left eye Removal was attempted but the tumor recurred after surgical excision

M K a healthy [illegible]0 year old woman had several cafe au lait spots One was clearly visible on the left side of the neck below the angle of the jaw The others were on the trunk She had no skin tumors nor neurological symptoms She was married but had no children

Dor K a 16 year old girl had developed headaches and left hemiparesis insidiously over a period of several months Eighteen months before she came under our observation a posterior craniotomy was performed and a small tumor of the brainstem was found Pathological diagnosis was spongioblastoma polare Post operative roentgen radiation was given She gradually improved so that at the time we saw her her activities were perfectly normal for a girl of her age and she was obtaining excellent grades in high school At the age of 16 she had not menstruated Numerous cafe au lait spots were present on the trunk the gluteal regions and the back of the neck. There were no skin or nerve trunk tumors There was no weakness of the extremities

All other members of the family were free from signs of multiple neurofibromatosis No mental defect or nerve deafness was found in this family

Related Disorders

Several multiple neoplastic syndromes which bear a similarity to neurofibromatosis have been classified under the general heading of neuro ectodermal dysplasia Whether the neuro-ectoderm is the tissue at fault in all these conditions is questionable but the term is nevertheless descriptive because of the occurrence of the lesions predominantly in the nervous system and in the skin Lesions of these syndromes have been found in patients affected with neurofibromatosis but their exact relation to the latter disease is not clear Inasmuch as the clinical picture in each of these conditions is rather clearly defined it will be of interest to consider them briefly at this time

Tuberous sclerosis is perhaps the most closely related to von Recklinghausen s disease At least sclerotic patches in the brain resembling those seen in this disease are also sometimes found in central neurofibromatosis These lesions were described by Bourneville in 1880 in a fifteen year old girl who had mental deficiency associated with hemiplegia and Jacksonian epilepsy[3] She had an undiagnosed eruption on the nose cheeks and forehead In addition numerous small mollusca were present on the neck The left leg was longer and larger than the right At autopsy islands of sclerosis were found scattered diffusely over the cerebral convolutions In other cases bilateral small cystic tumors of the kidneys have been noted Rhabdomyomas of the heart are seen with tuberous sclerosis and rarely without it Tumors of the thyroid thymus

D H K had cafe au lait spots on the trunk which were called grease spots by members of the family He had no known tumors At the age of 50 he died suddenly from a massive upper gastrointestinal hemorrhage His health was said to be perfect up to that time

W K a 6- year old man had numerous typical cafe au lait spots and soft elevated molluscoid tumors One tumor the size of a lemon protruded from the left costal margin He complained of epigastric pain relieved by food of weight loss and of constant pain in the left costovertebral angle Carcinoma of the stomach was suspected but not proved by extensive x ray studies He had some diminution of hearing in the left ear, but this was not due to nerve involvement

O K brother of W K had local gigantism of second left toe and cafe au lait spots from infancy In 19 4 he had symptoms of a cerebellar tumor A posterior decompression was performed at that time but no tissue was removed X ray therapy was given following operation The patient showed marked improvement and led a practically normal life for 3 years He was seen in April 1947 for pain in the left thorax and arm He had numerous molluscoid skin lesions and cafe au lait spots A tumor was seen in the right fossa of Rosenmuller and on excision proved to be a neurofibroma X-ray examination showed a large mass in the apex of the left chest Surgical removal of this mass was attempted but was unsuccessful because of the involvement of mediastinal structures Pathological examination showed the tumor to be a carcinoma rather than a neurofibrosarcoma as was expected The patient died August 1947 at the age of 48 Autopsy confirmed the surgical diagnosis of carcinoma of the lung and metastases were found in the brain and adrenals Gliotic patches in the brain similar to those found in tuberous sclerosis were present There was a 3 × 3 × 1 centimeter cyst in the left cerebellar hemisphere and there were smaller cysts in the optic radiation in the cortex of both kidneys and in the liver which raised the question of Lindau s syndrome although no angioma was found in the wall of the cerebellar cyst The patient also had a basal cell carcinoma of the skin overlying the sternum

L K a 4- year old man had cafe au lait spots A single plexiform neuroma arose from the forehead and left upper eyelid This tumor had occluded the vision of the left eye since childhood so that there was no vision in the left eye Removal was attempted but the tumor recurred after surgical excision

M K a healthy 20 year old woman had several cafe au lait spots One was clearly visible on the left side of the neck below the angle of the jaw The others were on the trunk She had no skin tumors nor neurological symptoms She was married but had no children

Another type of vascular tumor syndrome is *Sturge-Weber's disease*.[101] It is distinguished by nevus flammeus (port wine stain) of the face and other parts of the body, idiocy, paresis, epilepsy and visual disorders. Pathologically there are cerebral hypoplasia, hypogyria, cortical calcifications, telangiectases of the pial vessels and buphthalmos. Characteristically the port wine stain follows the distribution of the trigeminal nerve and there is a massive hemangioma involving the meninges on the same side of the head producing a contralateral hemiparesis. It has been shown that incomplete variants occur. Worster-Drought and Dickson have included also in this general group other multiple neoplastic syndromes, for example, myxo-chondro-adenoma of the base of the skull associated with cavernous angioma of the brain.[10]

Some authors have attempted to add such widely varying diseases as *scleroderma, painful lipomatosis, Albright's syndrome* and even the *lipoidoses*. We do not believe that the evidence at present is complete enough to justify this. While the disorders described in this section bear a certain similarity to von Recklinghausen's disease and some have been found in the same family and even in the same individual, the genetic evidence is against their arising from the same defective gene. Indeed each of the syndromes seems to be transmitted separately and their concurrence is rare. In our opinion it is safer at present to look upon multiple neurofibromatosis as a distinct and specific clinical entity.[103, 104]

Prognosis

Harbitz stated "the patients die with the disease and not from it."[40] Persons with von Recklinghausen's disease have lived more than eighty years with no greater complaint than the unpleasant appearance of their skin tumors. Nevertheless the prognosis must be guarded for several reasons. Of greatest importance is the fact that an estimated 1[illegible] to 13 per cent of patients develop malignant lesions.[1, 5, 106, 10] These in the main are slowly growing neurofibrosarcomas which do not metastasize until late and involve contiguous structures only by direct extension along nerve trunks. However, death from lung metastases has occurred from relatively small sarcomas. In general the larger and more rapidly *growing tumors are most likely to be malignant. Seldom will it be found* that a superficial tumor under 5 centimeters in diameter is a sarcoma.

Excision of a peripheral neurofibrosarcoma of a low grade of malignancy may be followed by a more malignant recurrence. Repeated

breast and duodenum have been reported The common accompaniment of tuberous sclerosis is *adenoma sebaceum* of the skin, and persons with the latter lesion are nearly always of subnormal intelligence *Adenoma sebaceum* is a tumorous developmental anomaly, usually coming on early in life It consists of numerous, small, closely-set tumors, symmetrically disposed on the face, chiefly on and about the nose, chin and forehead These tumors are sebaceous nevi of nerve or nerve sheath origin and thus are related to neurofibromas As described by Fowler and Dickson[96] the tuberous lesions in the brain are nodular and hard, embedded in the cerebral hemispheres and more easily felt than seen Microscopically they appear as patches of gliosis containing degenerating large cells often multinuclear Orzechowski and Nowicki studied an 18 year old girl who had peripheral and central neurofibromatosis (meningiomas and intracranial neurofibromas)[47] At autopsy gliotic brain lesions similar to those of tuberous sclerosis were demonstrated She did not have adenoma sebaceum Similar patients have been observed by others There have also been a few reports of adenoma sebaceum and neuro fibromatosis in the same individual[48] A very few families have been observed in which tuberous sclerosis occurred in one member and von Recklinghausen's disease in another In 1933 Critchley reiterated the view of previous writers that the two diseases are closely related

If it be true, as Trotter maintains [0], that defective insulation of nerve fibers is the cause of the overgrowth of connective tissue to form neuro fibromas, it is reasonable to suppose that the growth of contiguous blood vessels might be similarly stimulated to form *multiple hemangiomas* Diseases of this sort are known and have been grouped by Beattie and Dickson with neurofibromatosis and tuberous sclerosis[98] In 1911 von Hippel described angiomas of the retina[99], but it was not until 19 6 that Lindau correlated these with cysts of the cerebellum in whose walls it was often possible to demonstrate hemangiomas and gliomas[100] Asso ciated malformations and tumors included cysts of the pancreas and kidneys and "hypernephromas" of the kidneys and adrenal glands Lindau compared these to coordinated growths of the somatic organs in tuberous sclerosis He stated that the tumors of the kidneys and adrenals were of a "benign hypernephroid" type and that the multiple cysts of the pancreas and kidneys were not of angiomatous origin He also re marked on the occurrence of hemangiomas of the spinal cord and cavernous angiomas of the skin About 20 per cent of the cases were noted by him to be familial Three generations were affected in two different family groups

abdominal pelvic or thoracic regions. Many surgeons and pathologists feel that there is danger of inciting the tumors to malignant change by local excision and ordinarily the tumors should be let alone. It is even debatable if large plexiform neuromas should be attacked for the comfort of the patient. One must be guided somewhat in the individual case by the desires of the patient of course. Certainly repeated local excisions are often followed by repeated overgrowth and not infrequently by the appearance of sarcoma.

Radiation therapy is of no value in the treatment of neurofibromas and neurofibrosarcomas because these peripheral lesions are radioresistant[6, 65, 69]. It might be helpful to irradiate the regions of surgical excisions with the hope of retarding the almost constant recurrences of neurofibromas. The most common intracranial lesions, meningiomas and acoustic neurofibromas, also are refractory to irradiation[65, 108]. On the other side of the ledger marked improvement has followed heavy irradiation of spongioblastoma polare complicating von Recklinghausen's disease. This has been shown by asymptomatic periods up to five years or more following only partial excision of such tumors with post-operative roentgen therapy[69]. While other intracranial and intraspinal lesions of the disease are generally insensitive, a symptom-free period of twenty-seven years followed x-radiation of a cerebellar lesion in one of our patients (see family K., individual O. K.). At autopsy the lesion proved to be a cerebellar cyst similar to those described in Lindau's syndrome. A thorough consideration of radiotherapy of the central lesions of neurofibromatosis is given by Dyke and Davidoff[63].

Hormonal therapy has been used in cases where obvious endocrine abnormalities coexist. Such measures have improved the associated condition but have uniformly failed to alter the course of formation of neurofibromas. In a disorder in which the appearance and increase in the size and number of lesions is so whimsical it is difficult to evaluate therapeutic results. It suffices to say that of the numerous forms of definitive treatment, both local and systemic, which have been attempted none is worth serious consideration.

Craigie's words of a hundred years ago are still applicable: "In the instance of Chronic Molluscum I fear little can be done either in the way of cure or palliation. The warm bath and keeping the skin as clean as possible by washing and its secretions in as good a state as may be practicable by gentle friction seem to embrace all the remedial means of which the disease admits."[2]

removals have been reported, finally requiring amputation of an extremity, which does not always prevent the further spread of the sarcoma[9] (see Case 4) It is noteworthy that the molluscoid lesions seldom if ever undergo malignant degeneration, while the deeper tumors of nerve trunks and visceral nerves have a much greater propensity to do so[6]

The intracranial and intraspinal tumors occurring in generalized neurofibromatosis present the same prognostic outlook as the same tumors occurring alone The mere multiplicity of these lesions for example, meningiomas however, decreases the chance of complete surgical cure and the chance of recurrence in this condition is much increased

Aside from the possibility of malignant changes it must be remembered that neurofibromas of the gastrointestinal tract may ulcerate leading to fatal hemorrhage, those of the bladder may do the same Lesions involving vital structures such as those of the mediastinum may be surgically irremovable Intracranial tumors may kill by occluding the cerebrospinal fluid pathways

The tumors of peripheral nerves seldom cause muscular paralysis or atrophy, but occasionally they do Their tendency to recurrence makes the results of nerve grafting uncertain These tumors may infrequently cause intractable pain which usually is relieved by local excision

Although the endocrine crises of life, especially puberty and pregnancy, are noted to cause an increase in the number and rate of growth of neurofibromas they do not always do so Thus it is impossible in the individual case to predict the course of the disease It is of some importance to know, as we have previously pointed out, that certain families have a predisposition to particular types and distributions of tumors The best rule however is to consider the prognosis as precarious in multiple neurofibromatosis including formes frustres as well

Treatment

There is no specific therapy for multiple neurofibromatosis other than surgical excision of the individual tumors This should be undertaken only when the lesions produce pain or interfere seriously with the activities of the patient[7] The intracranial and intraspinal lesions must of course be removed for pressure symptoms if it is possible to approach them This applies equally to tumors obstructing vital structures in the

13 THIEBIERGE G Un cas de maladie de Recklinghausen (neuro fibromatose generalisee) sans fibromes cutanes ni fibromes nerveux Bull et Mem de Soc med d Hop de Paris 1898 35 XV 143
14 FEINDEL E Sur les formes incompletes de la neurofibromatose Gaz hebd de Med et de Chir 1898 s III 877
15 FEINDEL E and OPPENHEIM R Sur les formes incompletes de la neurofibromatose Arch gen de Med 1898 II 77
16 THOMSON H A On Neuroma and Neurofibromatosis Turnbull and Spears Edinburgh 1900
17 PENFIELD W The encapsulated tumors of the nervous system Meningeal fibroblastomata perineural fibroblastomata and neuro fibromata of von Recklinghausen Surg Gyn and Obst 1927 XLV 177
18 PENFIELD W and YOUNG A W The nature of von Reckling hausen s disease and tumors associated with Arch Neurol and Psychiat 1930 XXIII 320
19 PENFIELD W Tumors of the sheaths of the nervous system in Cytology and Cellular Pathology of the Nervous System vol III Hoeber New York 1932
0 TROTTER W The insulation of the nervous system Brit Med Jour 19 6 II 103
1 VEROCAY J Zur Kenntnis der Neurofibrome Beitr z path Anat u z allg Path 1910 XLVIII 1
NAGEOTTE J Sheaths of the *peripheral nerves Nerve degen* eration and regeneration in Cytology and Cellular Pathology of the Nervous System W Penfield editor vol III p 955 Hoeber New York 1932
23 MURRAY M and STOUT A P Schwann cell versus fibroblast as the origin of the specific nerve sheath tumor Am Jour Path 1940 XVI 41
4 MASSON P Experimental and spontaneous schwannomas (periph eral gliomas) Am Jour Path 193 VIII 367
25 MASSON P Tumeurs encapsulees et benignes des nerfs Rev canad de Biol 1942 I 09
6 LHERMITTE J and DUMAS R La ganglio neuromatose dis seminee type anatomique du syndrome de Recklinghausen Rev Neurol 1926 XXX 579
27 ANTONI N R E Ueber Ruckenmarkstumoren und Neurofibrome Studien zur Pathologischen Anatomie und Embryogenese Berg mann Munich 19 0
8 YAKOVLEV P I and GUTHRIE R H Congenital ectodermoses (neurocutaneous syndromes) in epileptic patients Arch Neurol and Psychiat 1931 XXVI 1145

The disease is hereditary The only way of preventing it is by restriction of reproduction of affected persons, and even then the occurrence of mutations still must be expected

BIBLIOGRAPHY

1 TILESIUS, W G Historia Pathologica Singularis Cutis Turpitudinis Leipzig, 1793, quoted by von Recklinghausen[10] and Craigie

2 CRAIGIE D Account of an instance of molluscum chronicum (described in 1819) Edinburgh Med and Surg Jour 1851, LXXV, 105

3 BARKOW Bemerkungen uber die Nervenanschwellungen Nov Act physic Med 1829 XIV 2 quoted by Worster Drought and associates[4]

4 WORSTER DROUGHT C DICKSON W E C and McMENEMEY W Multiple meningeal and perineural tumors with analogous changes in the glia and ependyma (neurofibroblastomatosis) Brain 1937 LX 106

5 JACOBOVICS M Du molluscum Recherches critiques sur les formes, la nature, et le traitment des affections cutanees de ce nom suivies de la description detaillee d une nouvelle variete, presentee a l'Academie Royale des Sciences de Paris Pesth 1840, reviewed by Craigie

6 VIRCHOW R Ueber die Reform der pathologischen und therapeutischen Anschauungen durch die mikroscopischen Untersuchungen Virch Arch f path Anat 1847, I, 226

7 SMITH R W A Treatise on the Pathology Diagnosis and Treatment of Neuroma, Hodges and Smith Dublin, 1849 quoted by Fulton[8]

8 FULTON J H Robert W Smith s description of generalized neurofibromatosis New Eng Jour Med, 1929 CC 1315

9 HITCHCOCK A Some remarks on neuroma, with a brief account of three cases of anomalous cutaneous tumors in one family, Am Jour Med Sci 1862 XLIII 320

10 von RECKLINGHAUSEN F D Ueber die Multiplen Fibrome der Haut und ihre Beziehung zu den Multiplen Neuromen, Hirschwald Berlin 1882

11 MARIE P Leçons de Clinique Medicale (Hotel Dieu 1894 95) p 4 Masson et Cie Paris 1896

12 MARIE P and BERNARD A Presentation d un malade atteint de neurofibromatose generalisee Bull et Mem de Soc med d Hop de Paris 1896 3s XIII 00

13 THIEBIERGE G Un cas de maladie de Recklinghausen (neuro fibromatose generalisee) sans fibromes cutanés ni fibromes nerveux Bull et Mém de Soc med d Hop de Paris 1898 3s XV 143
14 FEINDEL E Sur les formes incompletes de la neurofibromatose Gaz hebd de Med et de Chir 1898 s III 877
15 FEINDEL E and OPPENHEIM R Sur les formes incompletes de la neurofibromatose Arch gen de Med 1898 II 77
16 THOMSON H A On Neuroma and Neurofibromatosis Turnbull and Spears Edinburgh 1900
17 PENFIELD W The encapsulated tumors of the nervous system Meningeal fibroblastomata perineural fibroblastomata and neuro fibromata of von Recklinghausen Surg Gyn and Obst 19 7 XLV 177
18 PENFIELD W and YOUNG A W The nature of von Reckling hausen s disease and tumors associated with Arch Neurol and Psychiat 1930 XXIII 3 0
19 PENFIELD W Tumors of the sheaths of the nervous system in Cytology and Cellular Pathology of the Nervous System vol III Hoeber New York 193
0 TROTTER W The insulation of the nervous system Brit Med Jour 19 6 II 103
1 VEROCAY J Zur Kenntnis der Neurofibrome Beitr z path Anat u z allg Path 1910 XLVIII 1
2 NAGEOTTE J Sheaths of the peripheral nerves Nerve degen eration and regeneration in Cytology and Cellular Pathology of the Nervous System W Penfield editor vol III p 955 Hoeber New York 193
23 MURRAY M and STOUT A P Schwann cell versus fibroblast as the origin of the specific nerve sheath tumor Am Jour Path 1940 XVI 41
4 MASSON P Experimental and spontaneous schwannomas (periph eral gliomas) Am Jour Path 193 VIII 367
25 MASSON P Tumeurs encapsulees et beneignes des nerfs Rev canad de Biol 1942 I 209
6 LHERMITTE J and DUMAS R La ganglio neuromatose dis seminee type anatomique du syndrome de Recklinghausen Rev Neurol 1916 XXX 579
7 ANTONI N R E Ueber Ruckenmarkstumoren und Neurofibrome Studien zur Pathologischen Anatomie und Embryogenese Berg mann Munich 19 0
8 YAKOVLEV P I and GUTHRIE R H Congenital ectodermoses (neurocutaneous syndromes) in epileptic patients Arch Neurol and Psychiat 1931 XXVI 1145

9 SCHROEDER C H Beitrag zur Vererbung der Recklinghausen schen Neurofibromatose Beitr z klin Chir, 1936 CLXIV, 565

30 SUTTON R L and SUTTON R L, Jr Diseases of the Skin, 10th ed p 628 Mosby St Louis 1939 and Synopsis of Diseases of the Skin, p 355 Mosby St Louis 194-

31 PREISER S A and DAVENPORT, C B Multiple neurofibromatosis and its inheritance with description of a case Am Jour Med Sci, 1918 CLVI 507

3 HUXLEY J Evolution The Modern Synthesis chap 3 Allen and Unwin London 194

33 BRUNS, P Das Ranken-Neurom, Virch Arch f path Anat 1870 L 80

34 GENERSICH A Multiple Neurome Virch Arch f path Anat 1870, XLIX, 15

35 MURRAY J On three cases of a peculiar form of molluscum in children Lancet, 1873 I 410

36 CZERNY V Eine Elephantiasis Arabum Congenita 1874 quoted by Preiser and Davenport[31]

37 HERCZEL E Ueber Fibrome und Sarcome bei peripheren Nerven Beitr z path Anat u z allg Path 1890 VIII 38

38 SALOMON G Multiple Neurom bei einem Schwachsinnigen Individium Charite Annalen 1877 IV, 133, quoted by Preiser and Davenport[31]

39 SUTHERLAND A Case of (?) von Recklinghausen s disease Clin Soc Trans 1906 XXXIX, 245

40 HARBITZ F Multiple neurofibromatosis (von Recklinghausen s disease) Arch Int Med 1909 III 33

41 ARNOZAN A and PRIOLEAU L Sur les dermatofibromes congenitaux generalises Ann de Dermat et Syph, 1883 s IV 689

4 GARDNER W J and FRAZIER C H Bilateral acoustic neurofibromas Arch Neurol and Psychiat 1930 XXIII 66

43 CORNIL L KISSEL P BEAU A and ALLIEZ J Les formes generalisees et dissociees de la maladie de Recklinghausen (neuro ectodermomatose) Presse med 1933 XLI 2077

44 VAN BOGAERT L Les dysplasies neuro ectodermiques congenitales Rev Neurol 1935 LXIII 353

45 CRITCHLEY M and EARL C T C Tuberous sclerosis and allied conditions Brain 193 LV 311

46 URBACH L and WIEDMANN A Morbus Pringle and Morbus Recklinghausen Ihre Beziehungen zueinander Arch f Dermat u Syph 19 9 CLVIII 334

47 ORZECHOWSKI K and NOWICKI W Zur Pathogenese und pathologischer Anatomie der multiplen Neurofibromatose und der Sclerosa tuberosa (Neurofibromatosis universalis) Zeitschr f d ges Neurol u Psychiat 191 XI 37
48 SKFER J Adenoma sebaceum (Pringle) von Recklinghausen s disease subungual fibromatosis associated with epilepsy or tuberous sclerosis Symptom complex Urol and Cutan Rev 1938 XLII 110
49 GAMPER E Zur Kenntnis der zentralen Veränderungen bei Morbus Recklinghausen Jour f Psychol u Neurol 19 9 XXXIX 39
50 MILK F A case of neurofibroma (disease of Recklinghausen) Boston Med and Surg Jour 1905 CLII 370
51 SHARPE J C and YOUNG R H Neurofibromatosis The effect of pregnancy on the skin manifestations Jour Am Med Assoc 1936 CVI 682
52 SUTTON R L A clinical note on fibroma molluscum gravidarum Am Jour Obst 1911 LXIII 56
53 TRAENKEL J and HUNT J On neurofibromatosis Med Record 1903 LXIII 9 6
54 ROLLESTON J D and MACNAUGHTON N S Familial von Recklinghausen s disease Rev Neurol and Psychiat 1912 X 1
55 WEBER F P and PERDRAU J R Periosteal neurofibromatosis Quart Jour Med 19 9 30 XXIII 151
56 PAGET J Lectures on Surgical Pathology 3rd Am ed p 510 Lindsay and Blakiston Philadelphia 1865
57 GRINKER R Neurology 3rd ed p 4 Thomas Springfield 1943
58 COCKAYNE E A Inherited Abnormalities of the Skin and its Appendages p 74 Oxford Univ Press London 1933
59 FELDMAN W H Neoplasms of Domesticated Animals p 8 Saunders Philadelphia 193
60 LUCKE B Tumors on the nerve sheaths in fish of the snapper family (lutjanidae) Arch Path XXXIV 133
61 BILLOW B W Von Recklinghausen s neurofibromatosis A case of hepatomegaly and splenomegaly Am Jour Surg 1943 LXI 1 8
6 BIELSCHOWSKY M and ROSE M Zur Kenntnis der zentralen Veraenderungen bei Recklinghausenschen Krankheit Jour f Psychol u Neurol 19 7 XXXV 4
63 WEIL A Textbook of Neuropathology nd ed p 286 Grune and Stratton New York 1945
64 HASSIN G B Histopathology of the Peripheral and Central Nervous Systems nd ed pp 60 484 Hoeber New York 1940
65 EWING J Neoplastic Diseases a Treatise on Tumors 4th ed p 159 Saunders Philadelphia 1940

66 BOYD W Textbook of Pathology, 4th ed, p 907 Lea and Febiger Philadelphia 1943 also Surgical Pathology, 6th ed p 664 Saunders Philadelphia 1947
67 BIELSCHOWSKY M Familiare hypertrophische Neuritis und Neurofibromatose Jour f Psychol u Neurol 1922, XXIX 18
68 EWING J The structure of nerve tissue tumors with reference to radium therapy Proc Assoc Res in Nerv and Ment Dis, 19 1 LIII 130
69 DYKE C G and DAVIDOFF L M Roentgen Treatment of Diseases of the Nervous System Lea and Febiger Philadelphia 1942
70 MOORE R A A Testbook of Pathology p 1-10 Saunders Philadelphia 1945
71 MASSON P Les naevi pigmentaires tumeurs nerveuses, Ann d Anat et Path, 19-5 III, 417 & 657
7- CUSHING H Tumors of the Nervus Acousticus and the Syndrome of the Cerebellopontine Angle, Saunders, Philadelphia 1917
73 HEUER G The so called hour-glass tumors of the spine, Arch Surg 19-9 XVIII, 935
74 WISHART J H Case of tumors in the skull dura mater, and brain Edinburgh Med and Surg Jour, 18 2, XVIII ,93
75 ROUSSY G and OBERLING C Les tumeurs angiomateuses des centres nerveux Presse med 1930 XXXVIII 179
76 BROOKS B and LEHMAN, E P The bone changes in Recklinghausen s neurofibromatosis, Surg, Gyn and Obst, 19 4 XXXVII 587
77 CHANDLER F Local overgrowth Jour Am Med Assoc 1937 CIX 1411
78 MOORE B Some orthopaedic relationships of neurofibromatosis Jour Bone and Joint Surg 1941 XXXIX 109
79 ASHTON L P A case of von Recklinghausen s disease (multiple neurofibromatosis) with spontaneous fractures Bristol Med Surg Jour 1930 XLVII 219
79a WELCH C S ETTINGER, A and HECHT P L Recklinghausen s neurofibromatosis associated with intrathoracic meningocele New Eng Jour Med 1948 CCXXXVIII 6--
79b CROSS G O REAVIS J C and SAUNDERS W W Intrathoracic meningocele A case report to appear in Jour Neurosurg
80 COHEN R and DOUADY D Coexistence des deux maladies de Recklinghausen chez un sujet Presse Med 1936 XLIV 063
81 THANNHAUSER S J Neurofibromatosis (von Recklinghausen) and osteitis fibrosa cystica localisata et disseminata (von Recklinghausen) Medicine 1944 XXIII 105

82 von RECKLINGHAUSEN F D Die fibroese oder deformierende Ostitis Osteomalacie und osteoplastische Carcinose Berlin 1891 quoted by Thannhauser[41]

83 ALBRIGHT, F BUTLER A M HAMPTON A O and SMITH P Syndrome characterized by osteitis fibrosa disseminata areas of pigmentation and endocrine dysfunction with precocious puberty in females New Eng Jour Med 1937 CCXVI 7 7

84 BRENNER F, KONZETT H and NAGL, F Pheochromocytoma der Nebennieren mit Neurofibromatose Muench med Wochnschr 1938 LXXXV 914

85 HALPERN S and FASHENA G Von Recklinghausen s disease with diabetes mellitus Jour Clin Endocrin 1941 I 7 6

86 GORDON M B An endocrine consideration of Recklinghausen s disease report of a case associated with childhood myxedema Endocrinology 19 9 XIII 551

87 LEVIN O L and BEHRMAN H T Recklinghausen s disease Its elusive manifestations and internal relations Arch Derm and Syph 1940 XLI 480

88 van der HOEVE, J Eye symptoms in phakomatoses Doyne Memorial Lectures Trans Ophth Soc U K 193 LII 380

89 LYLE, D J Neuro-ophthalmology p o Thomas Springfield 1945

90 ADAIR F E and McLEAN J Tumors of the peripheral nerve system in Tumors of the Nervous System vol XVI chap xii Assoc Res in Nerv and Ment Dis Williams and Wilkins Baltimore 1937

91 MIMPRISS T W Neurofibroma of stomach in von Recklinghausen s disease Proc Roy Soc Med 1947 XL, 1 0

9 CHAUFFARD A Dermato fibromatose pigmentaire (ou neurofibromatose generalisee) Bull et mem Soc med d Hop de Paris 1896 XIII 777

93 WEBER F P A note on the relations of capillary haemangiectatic naevus and naevus anaemicus to the nervous system Brit Jour Derm and Syph 19 9 XLI 1

94 ELWYN H Diseases of the Retina p 331 Blakiston, Philadelphia 1946

95 BOURNEVILLE Contribution a l etude de l idiotie Arch de Neurol 1880 I 69

96 FOWLER J S and DICKSON W E C Tuberous (tuberose) sclerosis Quart Jour Med 1910 IV 43

97 CRITCHLEY M Tuberose sclerosis (epiloia) Med Annual 1933 p 511

98 BEATTIE, J M and DICKSON W E C A Textbook of Pathology General and Special p 1135 Heinemann London 1943

66 BOYD W Textbook of Pathology 4th ed, p 907 Lea and Febiger Philadelphia 1943 also Surgical Pathology, 6th ed p 664 Saunders Philadelphia 1947
67 BIELSCHOWSKY M Familiare hypertrophische Neuritis und Neurofibromatose Jour f Psychol u Neurol 19?, XXIX 18
68 EWING, J The structure of nerve tissue tumors with reference to radium therapy Proc Assoc Res in Nerv and Ment Dis 19?1 LIII, 130
69 DYKE C G and DAVIDOFF L M Roentgen Treatment of Diseases of the Nervous System Lea and Febiger Philadelphia 194
70 MOORE R A A Testbook of Pathology, p 1?10 Saunders Philadelphia 1945
71 MASSON, P Les naevi pigmentaires tumeurs nerveuses Ann d Anat et Path, 192?, III 417 & 657
72 CUSHING H Tumors of the Nervus Acousticus and the Syndrome of the Cerebellopontine Angle, Saunders Philadelphia 1917
73 HEUER G The so-called hour-glass tumors of the spine Arch Surg 19 9 XVIII 935
74 WISHART, J H Case of tumors in the skull dura mater, and brain, Edinburgh Med and Surg Jour 182 XVIII 393
75 ROUSSY G and OBERLING C Les tumeurs angiomateuses des centres nerveux Presse med 1930 XXXVIII 179
76 BROOKS B and LEHMAN, E P The bone changes in Recklinghausen s neurofibromatosis, Surg, Gyn and Obst, 19 4 XXXVII 587
77 CHANDLER F Local overgrowth Jour Am Med Assoc 1937 CIX 1411
78 MOORE B Some orthopaedic relationships of neurofibromatosis Jour Bone and Joint Surg 1941 XXIX 109
79 ASHTON L P A case of von Recklinghausen s disease (multiple neurofibromatosis) with spontaneous fractures Bristol Med Surg Jour 1930 XLVII 219
79a WELCH C S ETTINGER A and HECHT P L Recklinghausen s neurofibromatosis associated with intrathoracic meningocele New Eng Jour Med 1948 CCXXXVIII 6 2
79b CROSS G O REAVIS J C and SAUNDERS W W Intrathoracic meningocele A case report to appear in Jour Neurosurg
80 COHEN R and DOUADY D Coexistence des deux maladies de Recklinghausen chez un sujet Presse Med 1936 XLIV ?063
81 THANNHAUSER S J Neurofibromatosis (von Recklinghausen) and osteitis fibrosa cystica localisata et disseminata (von Recklinghausen) Medicine 1944 XXIII, 105

CHAPTER VII

DIPLEGIA

By A. GREIG ANDERSON

TABLE OF CONTENTS

Synonyms.—Congenital spastic paraplegia; Little's disease.

Under the general heading "diplegia" is included a variety of clinical conditions which have in common bilateral paralysis of varying extent and distribution of an upper motor neuron type, but which differ markedly both in etiology and in pathology.

There are two main groups of cases: one in which the condition is present at birth, due to causes acting during intrauterine life or during parturition; in the other, after a period of normal health the disease commences insidiously or abruptly and is due to developmental defect or degeneration of the upper motor neurons.

ETIOLOGY

The etiological factors are divided into three groups: (1) antenatal, (2) natal and (3) postnatal.

In the first of these groups the commonest is a history of continued ill health in the mother during pregnancy. Syphilis has long been supposed to be one of the most important causes, though until the introduction of the Wassermann reaction positive evidence was difficult to obtain. Only in a small percentage of cases was a parental history of syphilis obtained and

99 VON HIPPEL E Die anatomische Grundlage der von mir beschriebenen sehr seltenen Erkrankung der Netzhaut Arch f Ophth 1911, LXXIX, 350
100 LINDAU A Studien uber Kleinhirncysten Bau Pathogenese und beziehung zur Angiomatosis Retinae Acta Path et Microbiol Scand, supp I, p 1, Ohlsson Lund 19 6
101 WEBER F P A note on the association of extensive haemangiomatous naevus of the skin with cerebral (meningeal) haemangioma Proc Roy Soc Med 19 9 XXII 431
10- WORSTER-DROUGHT C and DICKSON W E C Venous angioma of the cerebrum Jour Neurol and Psychopath 19 7 VIII 19
103 CRITCHLEY, M and EARL C T C Tuberous sclerosis and allied conditions Brain 1932, LV 311
104 CAROL W L and VAN HEUSDEN J C Bourneville Pringles disease and Recklinghausens neurofibromatosis Arch f Dermat u Syph 1937 CLXXV, 1 abstracted in 1937 Year Book of Dermatology and Syphilology, p 241 The Year Book Publishers Chicago 1937
105 GARRÉ C Ueber secundar maligne Neurome, Beitr z. klin Chir 189 IX, 465
106 ADRIAN C Ueber die Neurofibromatose und ihre Komplicationen Beitr z klin Chir 1901 XXXI 1
107 HOSOI K Multiple neurofibromatosis with special reference to malignant transformation Arch Surg 1931 XXII -58
108 BAILEY P The results of roentgen therapy on brain tumors Am Jour Roentgenol and Rad Therapy, 19 5 XIII, 48

FEBRUARY 1 1950

metrically distributed over both cerebral hemispheres The convolutions are small and ill-developed the sulci are wide and deep Microscopically there is a deficiency of the nerve cells and fibers with overgrowth of the interstitial glial tissue The pyramidal tracts are undeveloped In other cases porencephalic defects are present These are of vascular origin and due to thromboses multiple hemorrhages or emboli Simple arrest of development of one cerebral hemisphere has also been found Various forms of meningitis may cause arrest of cerebral development In the atrophic type an extensive sclerosis of the frontal lobes without any affection of the cerebellum has been described in two cases by Foerster Clark has suggested that in this condition both cerebrum and cerebellum are involved

SYMPTOMS

The cases have been divided into groups according to the most prominent symptom present Thus the spastic the athetoid the choreic the atonic and the perverse movement groups are differentiated Many of the cases show symptoms of two or more of these groups so that no hard and fast division can be made

Spastic Type

The essential symptoms are rigidity muscular weakness contractures increased deep reflexes and a variable degree of mental deficiency In severe cases the attention of the mother or nurse may be directed to the undue rigidity of the limbs from the difficulty of washing and dressing the child In Little s phrase it is noted that the child can be turned over in its mother s lap all of a piece" As a rule the symptoms though present at birth do not become prominent till the time when the child should begin to sit up to talk and to walk He is late in learning to sit up and to walk and all h s movements are clumsy

The rigidity is much greater in degree than the muscular weakness and involves to a greater or less extent all the mu cles of the body It is most marked in the muscles of the lower limbs le s so in those of the upper limbs and least of all in the muscles of the face The thighs are rotated inwards and the knees pressed closely together from spasm of the adductors and of the internal rotators the knees are slightly flexed or extended and the feet maintained in the equinus or the cavus position The gait is stiff and clumsy and where the adductor spasm is more severe is typically cross legged or scissors like The spasticity though not so obvious in the upper limbs is shown in the awkwardness and clumsiness of all the finer movements Diffi culty in articulation and deglutition is common The affection of the mus

few of the cases showed definite stigmata of a congenital infection The percentage of positive reactions obtained in these cases varies considerably but Findlay and Robertson have recorded thirteen positive results in a small series of thirty three cases The importance of the serological examination not only of the patient but also of the parents and of the other members of the family has been already referred to in discussing the etiology of mental deficiency in children Injury to the mother during pregnancy may cause a meningeal hemorrhage in the fetus more especially in cases where vascular degeneration is already present due to congenital lues

In the second or natal group much importance has been attributed to prolonged and difficult labor necessitating interference by instrument or turning The prolonged pressure on the fetal head is believed to cause overlapping of the parietal bones leading to tearing of the veins emptying into the longitudinal sinus The proper development of the motor cortex is thus interfered with by the pressure of the blood clot That meningeal hemorrhage is a factor in a certain number of cases is demonstrated by the operative results of Cushing though generally speaking undue weight appears to have been attached to this cause Premature birth precipitate labor and asphyxia neonatorum are also regarded as causes

In the cases arising after a period of normal health there are two groups one in which the symptoms arise slowly and insidiously and the other in which the onset is abrupt with high temperature delirium and convulsions In the first group there is probably an inherent defect of the motor neurons as in the case quoted by Taylor where two children of a mother suffering from disseminated sclerosis became paraplegic in early life In the second group the condition has been attributed by Strumpell to an infective polio encephalitis In the cases where the disease has arisen in the course of or subsequent to the ordinary infective fevers it is probable that these acted merely as exciting causes Occasionally the symptoms suggest a vascular lesion such as embolism or thrombosis

Pathology

The pathological findings in cases of diplegia have been and still are the subject of much controversy That meningeal hemorrhage occurring during labor is responsible for a certain limited number of cases appears to be definitely proved by the operative results of Cushing In cases dying at a late stage of the disease it is impossible to correlate the pathological lesions present with any single cause such as hemorrhage The condition most frequently found is one of diffuse atrophic sclerosis It may affect the whole of the cerebral cortex or be limited to one region of the brain or sym

metrically distributed over both cerebral hemispheres The convolutions are small and ill-developed the sulci are wide and deep Microscopically there is a deficiency of the nerve cells and fibers with overgrowth of the interstitial glial tissue The pyramidal tracts are undeveloped In other cases porencephalic defects are present These are of vascular origin and due to thromboses multiple hemorrhages or emboli Simple arrest of development of one cerebral hemisphere has also been found Various forms of meningitis may cause arrest of cerebral development In the atrophic type an extensive sclerosis of the frontal lobes without any affection of the cerebellum has been described in two cases by Foerster Clark has suggested that in this condition both cerebrum and cerebellum are involved

SYMPTOMS

The cases have been divided into groups according to the most prominent symptom present Thus the spastic the athetoid the choreic the atonic and the perverse movement groups are differentiated Many of the cases show symptoms of two or more of these groups so that no hard and fast division can be made

Spastic Type

The essential symptoms are rigidity muscular weakness contractures increased deep reflexes and a variable degree of mental deficiency In severe cases the attention of the mother or nurse may be directed to the undue rigidity of the limbs from the difficulty of washing and dressing the child In Little's phrase it is noted that the child can be turned over in its mother's lap "all of a piece As a rule the symptoms though present at birth do not become prominent till the time when the child should begin to sit up to talk and to walk He is late in learning to sit up and to walk and all his movements are clumsy

The rigidity is much greater in degree than the muscular weakness and involves to a greater or less extent all the muscles of the body It is most marked in the muscles of the lower limbs less so in those of the upper limbs and least of all in the muscles of the face The thighs are rotated inwards and the knees pressed closely together from spasm of the adductors and of the internal rotators the knees are slightly flexed or extended and the feet maintained in the equinus or the cavus position The gait is stiff and clumsy and where the adductor spasm is more severe is typically cross legged or scissors like The spasticity though not so obvious in the upper limbs is shown in the awkwardness and clumsiness of all the finer movements Difficulty in articulation and deglutition is common The affection of the mus

cles of the face causes loss of all emotional play producing a characteristic starched or spastic face The palpebral fissures are widened and the angles of the mouth retracted

The muscular rigidity gives rise to certain characteristic attitudes, i.e. the cramped attitude where the child occupies the least possible space, the attitude of adoration and the extension supination position"

Athetoid Type

The movements of athetosis are slow irregular, twisting worm like movements affecting mostly the peripheral parts of the limbs and more marked in the arms than in the legs In severe cases the movements start in one limb and spread successively to the other limb of the same side and to the arm and leg of the opposite side In bilateral athetosis the muscles of expression are involved producing overaction of the facial muscles and hideous grimacing The facial grimaces cause the child to appear much more mentally deficient than he really is The movements may occur spontaneously but are much increased on voluntary movement as a rule they cease during sleep In bilateral athetosis the rigidity may be very slight and the reflexes practically normal Hypertrophy of the muscles is not an infrequent result of athetosis but in severe cases without athetosis muscular wasting is the rule

Choreiform Type

The choreiform movements in diplegia are quick and shock like affecting the proximal parts of the limbs and rarely the face From time to time they become aggravated and may be so severe that the child is kept in bed with difficulty In cases where the rigidity is slight a definite intention tremor resembling that seen in insular sclerosis is sometimes observed

In certain cases of diplegia associated movements can be demonstrated Turning the patient's head passively to the right causes the left upper limb to be tonically flexed and the right upper limb to become extended Turning the head to the left reverses the movement

The amount of control over the sphincters depends on the mental condition present Common sensation is not affected

Atonic Type

The atonic type of diplegia is characterized by extreme hypotonia of the muscles and a severe degree of mental defect The child is unable to stand or walk or even sit up without assistance though voluntary movements are possible when the child is lying in bed The hypotonia allows of the limbs

being placed in all kinds of abnormal positions The tendon reflexes are present and the electrical reactions of the muscles are normal

Every degree of mental defect may be present from simple feeblemindedness to complete idiocy the amount of mental defect does not correspond with the degree of rigidity or paralysis Even the milder grades of diplegia are associated with considerable mental impairment Speech is learned late or not at all and in any case it is imperfect Complete blindness from cortical lesion or optic atrophy may be present Convergent strabismus occurs in a considerable number of cases and nystagmus has also been noted

Diagnosis

Cerebral diplegia may be distinguished from paraplegia of spinal origin by the absence of pain and anesthesia the presence of mental deficiency and other signs of cerebral disturbance and the history of the onset The choreic type may be confused with a simple chorea minor but the character and the persistence of the movements with the associated mental defect will serve to differentiate the two conditions True chorea minor is rare under the age of three years Cases with intention tremor may closely simulate disseminated sclerosis The diagnosis of the atonic type from the amyotonia congenita of Oppenheim is made on the condition of the reflexes and the electrical reactions of the muscles both of which are normal in the diplegic cases

Prognosis

The prognosis is unfavorable The disease in certain cases is progressive and little or nothing can be done to arrest the progress In others the condition is stationary and improvement up to a certain limited extent is possible but the child will remain permanently defective both mentally and physically The possibility of the onset of convulsions should be borne in mind

Treatment

The treatment is carried out on general lines Potassium iodid has been recommended and in cases where the Wassermann reaction has been found positive it would seem reasonable to try the effect of antispecific treatment with salvarsan Findlay has reported good results with neosalvarsan in a small number of cases of mental deficiency Cushing has operated upon four cases by trephining the skull and evacuating the blood clot with suc

cessful results in two cases Section of the posterior roots has also given good results in a small number of selected cases (Foerster) Tenotomy may be carried out for the correction of deformities but only in cases where the spasm is slight The mental education of the child should be carried out on the lines suggested for the treatment of mentally deficient children generally

BIBLIOGRAPHY

BATTEN F E and VON WYSS W H Brit Jour Child Dis Lond 1915 XII 65
COLLIER J S Brain Lond 1899 XXII 373
CUSHING H Am Jour M Sc Phila 1905 CXXX 563
FINDLAY L and ROBERTSON M E Glasgow M Jour 1914 LXXXII 401
FINDLAY L Glasgow M Jour 1914 LXXXII 241
FOERSTER O Deutsches Arch f Klin Med Leipz 1909 XCVIII, 216
LITTLE W J Tr Obst Soc Lond 1861–62 III 293
STEWART J P The Diagnosis of Nervous Diseases 5th ed London 1920
TAYLOR J Allbutt and Rolleston System of Medicine Phila and N Y 1911 VIII 452

CHAPTER VIII

HYDROCEPHALUS

BY A. GREIG ANDERSON

TABLE OF CONTENTS

Definition.—Hydrocephalus is a disease or rather a symptom of many diseases characterized by the presence of an excessive amount of cerebrospinal fluid within the cranial cavity. It may be congenital or acquired, primary or secondary, acute or chronic. The excess of fluid may be confined within the ventricular cavities (internal hydrocephalus) or within the subarachnoid spaces (external hydrocephalus).

PHYSIOLOGY OF CEREBROSPINAL FLUID

Since the excess of fluid may be determined by an increased production or by a diminished absorption, it is necessary to recapitulate briefly the physiology of the normal cerebrospinal fluid. The average amount of fluid is from 120 to 150 c.c. Although it resembles blood plasma and lymph in its inorganic constituents, it differs from them in its low specific gravity and in the absence of albumin and fibrinogen. The physical characters of the fluid are sufficient to distinguish it as a true secretion and to differentiate it from a simple exudate (Mott). Most

authorities are agreed that the cerebrospinal fluid is a true secretion from the ependymal cells lining the vascular choroid plexuses Cushing states that "certain experiments have shown that the cells may be definitely activated and the plexuses doubtless possess a definite glandular function Secretory granules have been demonstrated intra vitam by Francini and Levaditi The fluid may be secreted in large amount as has been frequently noted in cases of fracture of the base of the skull and in the cases of cerebrospinal rhinorrhea described by St Clair Thomson In a few such cases the fluid has amounted to one or two liters per day The fluid passes from the lateral ventricles through the foramen of Monro into the midventricular system whence it escapes into the general subarachnoid space through the foramina in the roof of the fourth ventricle From the subarachnoid space the fluid passes into the blood stream by direct communication with the dural sinuses (Cushing) the exact nature of the openings or channels being unknown Dandy and Blackfan believe that the absorption takes place from the entire subarachnoid cavity by a diffuse process of osmosis and that it is not restricted to any particular locality The process of absorption is similar to that which takes place from the peritoneal and pleural cavities It is probable that the Pacchionian bodies are not concerned in the process A small amount of fluid may possibly pass along the sheaths of the various cranial and spinal nerves and so gain access to the general lymph stream but the amount so disposed of is negligible

Classification

Since the pathology of hydrocephalus is but little known a classification of its different forms is attended with considerable difficulty and it has usually been made on purely symptomatic grounds It is usual to classify the various conditions as follows

I External Hydrocephalus

II Internal Hydrocephalus { A Congenital / B Acquired }

External Hydrocephalus

This is a rare condition Oppenheim includes under it all cases where there is an excess of cerebrospinal fluid within the subarachnoid space consequent on an atrophy of the brain such as occurs in phthisis or general paralysis hydrops e vacuo The majority of authors however restrict

the use of the term to those cases of congenital maldevelopment where a rudimentary brain is found in a cranial cavity of normal dimensions

Internal Hydrocephalus

The subdivision of internal hydrocephalus into congenital and acquired forms though not justified on pathological grounds is convenient on account of the different signs and symptoms produced in the child in whom the skull is readily distended and in the adult in whom ossification of the bones of the skull has already taken place In both groups a still further subdivision is often made into a primary or idiopathic form in which the pathology is still uncertain and a secondary form where the condition arises as the mechanical result of blockage by tumor or adhesions consecutive on meningeal inflammation It will be expedient to discuss first the pathology and pathogenesis of both groups

PATHOLOGY AND PATHOGENESIS

The congenital form has been attributed to trauma or mental excitement of the pregnant mother Syphilis cachexia and intoxications *e g* acute infections have been held accountable for some of the cases In certain families there seems to be an hereditary predisposition and several members of one family have been affected Congenital hydrocephalus is frequently accompanied by other abnormalities of the central nervous system such as spina bifida encephalocele etc or by abnormalities elsewhere *e g* clubfoot syndactyly etc The coincidence of hydrocephalus and spina bifida suggests that the normal closure of the central nervous system has been interfered with by an antenatal increase of pressure within the cranial cavity It is a common observation that an operation on a case of spina bifida may considerably increase any hydrocephalus already present

Occasionally meningeal thickenings are found in the region of the fourth ventricle indicating antenatal inflammation of the meninges but in the majority of cases no such obvious obstruction can be found The ependymal lining of the ventricles is frequently granular and there may be signs of inflammatory changes in the choroid plexuses The ventricles are widely dilated and the brain substance is reduced to a layer a few millimeters in thickness so that the brain comes to resemble a bag of fluid The fluid may amount to several liters The convolutions and the sulci are entirely obliterated the corpus callosum is reduced to a thin sheet of tissue the septum lucidum is frequently ruptured so that there is free communication between the lateral ventricles and the basal ganglia are rendered almost

unrecognizable The communications between the ventricles are also widely distended the foramen of Monro sometimes admitting three fingers The circumference of the skull is enormous The sutures are widely separated and the fontanelles distended and enlarged the bones are atrophic translucent and reduced to the thinness of parchment The frontal bones bulge over the face the temporal bones flare widely outwards The ridges separating the basal cranial fossae tend to become less prominent

The recent researches of Dandy and Blackfan have thrown much light on the difficult subject of the pathogenesis of this disease and have necessitated an entirely new classification Dandy gives it as follows

- Hydrocephalus due to
  - Diminished absorption of cerebrospinal fluid
    - Communicating hydrocephalus (due to adhesions in the subarachnoid space)
    - Obstructive hydrocephalus due to (1) Congenital Atresias (2) Adhesions { Acute, Chronic } (3) Tumors
    - External hydrocephalus?
  - Increased production of cerebrospinal fluid
    - Acute hydrocephalus (increased fluid from inflammatory products in acute meningitis and trauma)
    - Communicating hydrocephalus (due to occlusion of the vena magna Galeni)

They argue that if the cerebrospinal fluid is absorbed from the subarachnoid spaces by the Pacchionian bodies or by stomata opening into the dural sinuses the subarachnoid spaces in cases of so-called idiopathic hydrocephalus should be distended up to the point of the obstruction *i e* that the whole of the subarachnoid spaces over the cerebral hemispheres should be distended This argument holds good no matter whether we consider the cause of idiopathic hydrocephalus to be an increased production or a diminished absorption of the cerebrospinal fluid They state that this distention is not found in cases of idiopathic hydrocephalus but that on the contrary there is a diminution in the amount of fluid in the subarachnoid spaces over the cerebral hemispheres In these cases one is surprised by the absence of fluid in the sulci The sulci are obliterated and the separation of the convolutions is marked only by the vascular lines They believe as the result of their experimental investigations that the cerebrospinal fluid is absorbed from the whole of the subarachnoid spaces and especially from the subarachnoid spaces over the cerebral hemispheres which constitute four fifths of the total absorbing area The extraventricular circulatory system of the cerebrospinal fluid is compared to the trunk of a tree and its branches the basal cisterns representing the trunk and the subarachnoid spaces of the cerebral hemispheres corresponding

to the branches "*Adhesions encircling the midbrain where it passes through* the incisura tentorii will destroy all communications between the posterior and middle cranial fossae and thereby eliminate the entire subarachnoid space over both cerebral hemispheres from participation in the absorption of the cerebrospinal fluid Adhesions occluding the basal cisterns will be no less effective In other words adhesions in either of these regions *are equivalent to transection of the trunk of the tree To this type of hydro*cephalus they apply the name communicating Adhesions in the region of the cerebral hemispheres even if extensive will not have the same deleterious effect and hydrocephalus will not be produced or at least not to the same extent It is the situation of the adhesions and not their extent which is the important thing In a large series of cases of the communi*cating type the absorption of phenolsulphonephthalein from the sub*arachnoid space was found to be about one fifth of the normal

In the obstructive type of Dandy and Blackfan the obstruction occurs within the ventricular system and may be situated at any point from the lateral ventricles to the foramina in the roof of the fourth ventricle Between the communicating and the obstructive type of hydrocephalus therefore there is no essential difference except in the situation of the obstruction The varying surgical operations required to deal with the obvious anatomical differences justify the division of hydrocephalus into these two groups

Margulis in a recent study of six cases of acquired primary chronic internal hydrocephalus in adults and of four cases of secondary internal hydrocephalus concludes that the different varieties produce characteristic histological changes and that it is possible to diagnose the type of hydrocephalus present from the histological preparation alone The histological picture of a primary hydrocephalus shows a periependymal gliofibrosis This gliofibrosis is analogous to the spinal gliomatosis in cases of syringomyelia and is due to developmental disturbances of the glial tissue it may remain latent till secondary causes such as alcohol trauma and intercurrent illness lead to an increase of the intracranial pressure The chronic granular ependymitis is not an inflammatory process but belongs rather to the category of the scleroses and occupies a position midway between chronic inflammation and new growth formation

Congenital Hydrocephalus

Symptoms and Course

If the hydrocephalus has developed before birth there may be considerable difficulty in delivery and a certain number of these cases die during

birth More often the head at birth is of normal size from 35 to 40 centimeters in circumference but within the first few weeks o months a rapid and notable increase in size takes place so that the head may quickly attain a circumference of 80 to 100 centimeters It may increase by a centimeter a week or more The head is generally circular in shape but this depends on the degree of tension and on the habitual attitude assumed The extreme disproportion between the size of the head and that of the face the enormous bulging overhanging head and the tiny wizened face forms a striking and unmistakable picture The bones of the skull are thinned translucent and parchment like The fontanelles are widely distended and bulging the sutures gape widely the skin is tightly stretched over the bulging skull the hair is thin and scanty the veins are prominent and cord like the eyes are turned downwards by the pressure on the orbital plates the palpebral fissures are narrowed the sclera is exposed above the cornea the pupil is partly covered by the lower lid so that the child may have to pull the lower eyelid down to look at an object

As a rule there is great mental deficiency so that the majority of these children are idiots or imbeciles They learn to speak slowly or not at all In rare cases even though the hydrocephalic condition is well marked the mental faculties seem to be but slightly impaired In a very few exceptional cases where the process has come to a standstill at an early stage the individual has attained adult life with mental ability rather above than below the normal

Eye symptoms are not uncommon Optic neuritis and atrophy a e rare as one might expect from the readiness with which the skull becomes distended nystagmus has frequently been noted squint from ocular palsy is occasionally seen

The motor functions are usually impaired The legs are weak and may show a spastic condition with exaggerated knee jerks ankle clonus and extensor plantar reflexes The child is late in learning to walk and does so awkwardly the movements of the arms also are awkward and feeble often the head falls forward partly from its weight There may be incontinence of urine and feces In the more chronic type of case general convulsions are not uncommon and there may be attacks of severe headache and vomiting with rise of temperature

The cerebrospinal fluid sometimes makes its way outwards most often through the ethmoid bone into the nose intermittently or continuously "hydrorrhea nasalis or "rhinorrhea This is more common in acquired hydrocephalus Very rarely spontaneous perforation of the cerebral membranes occurs and escape of the cerebrospinal fluid through the sutures Lumbar puncture shows cerebrospinal fluid of normal appearance In rare cases the fluid may have a yellow color and clot spontaneously

The individuals are puny badly nourished and extremely liable to intercurrent infections so that comparatively few attain adult life and the majority succumb within the first few years

Diagnosis

The diagnosis as a rule presents little difficulty Confusion may arise between the milder grades of hydrocephalus and the large head of rickets In rickets the shape of the head tends to be square there is no bulging of the fontanelles brain symptoms are absent and rhachitic changes are present in the bones elsewhere The diagnosis of the type of hydrocephalus present and of the site of the obstruction if any is of extreme importance from the surgical point of view Dandy recommends the injection of one cubic centimeter of a specially prepared neutral solution of phenol sulphonephthalein into either ventricle A lumbar puncture is done half an hour later If an obstruction exists in the ventricular system the lumbar cerebrospinal fluid will remain colorless if the hydrocephalus is of the communicating type the drug passes freely into the lumbar cerebrospinal fluid but the absorption from the general subarachnoid space is very much delayed and the total quantity excreted in the urine is much less than normal

Treatment

Medical treatment is generally without effect Inunctions of mercury have been recommended and the exhibition of potassium iodid internally Compression of the skull by strips of adhesive plaster (Trousseau) or by broad elastic band has frequently been advocated this procedure is not without danger and in any case is of doubtful utility

Numerous operations all of them more or less dangerous have been proposed for the relief of this condition *e g* puncture of the lateral ventricle injection of iodin into the ventricles repeated lumbar puncture permanent drainage of the lateral ventricles into the subarachnoid space (and even into the peritoneum into the retroperitoneal spaces and into the pleural cavity) direct drainage into the sinuses of the brain by means of transplanted blood vessels drainage through the skull into the subcutaneous tissues More recently puncture of the corpus callosum has been recommended (Stetten and Roberts) Ligation of both common carotids has been performed Many of these procedures have been unsuccessful from failure to take account of the exact situation of the obstruction and others from a too rapid evacuation of the fluid from the ventricles Dandy has recorded the results of extirpation of the choroid plexuses in four cases of hydrocephalus of the communicating type Of these three

died two to four weeks after the operation One patient survived after a bilateral extirpation of the choroid plexus for a period of ten months and up to the time of publication the disease had showed no sign of advancing A full account of the various surgical operations suggested with a bibliography, is to be found in the papers of Kausch and Payr

Acquired Hydrocephalus

Acquired hydrocephalus may be divided into two groups (a) primary or idiopathic and (b) secondary *i e* consecutive to an attack of meningeal inflammation or due to the pressure produced by tumors

Primary Acquired Hydrocephalus

There is still a great deal of obscurity in regard to this variety but with the increasing refinements of histological methods there is a tendency for the number of primary or idiopathic cases to be reduced Gowers describes a form of acquired primary hydrocephalus which may appear at any age and in which no discoverable pathological lesion is present other than the slight traces of ventricular inflammation found in the congenital cases Oppenheim believes that a primary idiopathic hydrocephalus may occur in rare instances and he includes under the idiopathic cases the meningitis serosa of Quincke Cushing on the other hand regards all acquired hydrocephalus as secondary, and under the general heading "inflammations" he separates out two groups which we would rather regard as primary one due to ependymal inflammation and the other to serous meningitis He states earlier in his paper that if any meningitis can justly be regarded as primary it is the case characterized by an acute collection of fluid and associated with meningitis serosa and ependymitis Many of the cases described in literature such as those of Weber are secondary

Since the pathology is so obscure and the opinion of authorities is so varied we have adhered for the sake of simplicity to the classification of Gowers as indicated above and under primary acquired hydrocephalus we shall include the form associated with granular thickening of the ventricular lining membrane and the serous meningitis of the ventricles (Quincke) The latter form is analogous to the serous exudates of the pleural and peritoneal cavities and its onset is often associated with the acute infectious diseases such as typhoid pneumonia and otitis media

Symptoms of Primary Acquired Hydrocephalus.—The condition may develop acutely or chronically Where the onset is acute it may be exceedingly difficult to distinguish the condition from meningitis As a rule

the rise of temperature is slight or absent the rigidity of the neck is less well marked and the sight is usually very much affected The complete examination of the cerebrospinal fluid is of great value in the diagnosis The course of the disease is intermittent and many of the cases appear to terminate after a few weeks or months in more or less complete recovery It is not uncommon to find patients showing symptoms of an acute and severe brain disease (headache vomiting stupor and optic neuritis) which disappear completely within a few weeks or months leaving perhaps only permanent blindness (from postneuritic atrophy) to indicate the existence of previous brain disease

Where the onset is a chronic one the disease simulates very closely a brain tumor and is usually diagnosed as such There are the usual symptoms of headache vomiting stupor and optic neuritis with paralysis of various cranial nerves from compression

Certain ocular and visual symptoms may suggest hydrocephalus There is early impairment of the upward movement of the eyes and of the light reflex at a stage when the optic neuritis is acute and the vision unimpaired presumably due to the pressure of the third ventricle on the third nerve nucleus Bitemporal hemianopia from pressure on the optic chiasma is frequent There may be early failure of vision with the acute onset even of blindness where there is only acute papillitis present In some cases exophthalmos has been noted

Progressive spasticity of the limbs equal on the two sides with slight general weakness is common There is an absence of definite focal symptoms even if there is focal epilepsy one fit starts in an arm another in a leg in contrast to what occurs in a localized tumor

Occasionally even in the adult slight enlargement of the head has been noted The duration of the disease may extend over a period of years with intermissions and remissions

Secondary Acquired Hydrocephalus

Inflammation

Any inflammation of the base of the brain which leads to the closure of the foramina in the roof of the fourth ventricle will inevitably cause a condition of internal hydrocephalus Under the general discussion of the pathogenesis we have already seen the importance of the site of these adhesions Hydrocephalus is a frequent and fatal complication of both cerebrospinal and tuberculous meningitis Cushing calls attention to the importance of pyohydrocephalus as a terminal event in cerebrospinal menin

gitis Organisms may be found in the ventricular fluid long after they have disappeared from the lumbar spinal fluid In such cases the injection of antimeningococcic serum into the ventricles is indicated Flexner suggests that in certain of these cases the hydrocephalus may not be due to an actual organic block but that the lateral ventricles may be distended from a functional lack of resistance and that the downward pressure of the distended lower horns may cause a temporary occlusion of the outlet of the fourth ventricle Whytt in 1768 described the acute hydrocephalus of tuberculous meningitis and under that name the disease was for long described Thrombosis of the great vein of Galen and general venous thrombosis have been thought by some to play a part in the production of the acute hydrocephalic condition

Tumors

Tumors of the subtentorial region are especially prone to give rise to *an obstructive hydrocephalus by pressure on the fourth* ventricle or the aqueduct of Sylvius but the condition can be produced also by tumors of the cerebrum obstructing the foramen of Monro Hydrocephalus may occasionally be associated with tumors of the pituitary gland Cysticercus of the fourth ventricle is an extremely rare cause Tumors of the brain of a child where the skull has been greatly distended may readily be mistaken for congenital hydrocephalus The abrupt onset of pressure symptoms in cases of brain tumor is generally due to an obstructive hydrocephalus

BIBLIOGRAPHY

CUSHING H Osler and McCrae System of Medicine Phila and N Y 1910 VII 460
CUSHING H and SLADEN F J Jour Exper M N Y 1908 X 548
DANDY W E Ann Surg Phila 1918 LXVIII 569
DANDY W E and BLACKFAN K D Jour Am M Ass Chicago 1913 LXI 2216 Am Jour Dis Child Chicago 1914 VIII 406 and 1917 XIV 4 4
FLEXNER S Jour Am M Ass Chicago 1917 LXIX 817
GOWERS W R Diseases of the Nervous System Lond 1888 II 539
HAYNES I S *Ann Surg Phila 1913 LVII 449*
KAUSCH W Arch f klin Chir Berl 1908 LXXXVII 709
MARGULIS M S Arch f Psychiat Berl 1912-13 L 31
MOTT F W Allbutt and Rolleston System of Medicine Lond 1911 VII 266
OPPENHEIM H Lehrbuch der Nervenkrankheiten 5th ed Berl 1908
PAYR E Arch f klin Chir Berl 1908 LXXXVII 801
STETTEN D W and ROBERTS D Jour A M A Chicago 1919 LXXI 44
THOMSON St C Diseases of the Nose and Throat Lond 1912 19-
WEBER L W Arch f Psychiat Berl 1906 XII 64

CHAPTER IX

IDIOCY

By A GREIG ANDERSON

Table of Contents

Introduction

Mental deficiency in children may be divided into three grades the feebleminded the imbecile and the idiot according to the degree of mental defect present The definition of these terms adopted by the Royal Commission on "The Care and Control of the Feebleminded (1908) is

1 A feebleminded person is one who is capable of earning a living under favorable circumstances but is incapable from mental deficiency existing from birth or from an early age of (a) competing on equal terms with his normal fellows or (b) managing himself or his affairs with ordinary prudence

2 The imbecile is one who by reason of mental defect existing from birth or from an early age is incapable of earning his own living but is capable of guarding himself against common physical dangers

3 An idiot is one so deeply defective in mind from birth or from an early age that he is unable to guard himself against common physical dangers

A "moral imbecile" is one who displays early vicious or criminal tendencies which are of an incorrigible or unusual nature.

The lifelong nature of the disease and its incurability with the necessity for lifelong care and supervision should be emphasized. The child mentally backward by reason of chronic illness or lack of opportunity of training may be educated up to the standard of his normal fellows; the mentally deficient child, though capable of improvement and training up to a certain limited extent, can never be made normal. The statistics of the Commissioners' report show that at least 0.46 per cent. of the population are mentally defective.

Etiology

Mental deficiency occurs as a primary condition in ninety per cent. of cases, *i.e.* it is due to some inherent defect of the germ plasm leading to imperfect development, and as a secondary condition in ten per cent. of cases, *i.e.* due to some extraneous or accidental cause. There can be little doubt that in the group of primary cases the most important etiological factor is a neuropathic inheritance, under which is included a family history of insanity, epilepsy or mental deficiency. The Royal Commission concluded that feeblemindedness is usually spontaneous in origin, *i.e.* not due to influences acting on the parents, and tends strongly to be inherited. Much stress has been laid on alcohol as a potent factor, but its importance seems to have been considerably overrated. Chronic alcoholism in itself is in the majority of cases a symptom of mental instability and is associated with a certain amount of mental defect, and it is not surprising therefore that this mental instability should appear in the progeny of chronic alcoholics as a full blown mental deficiency.

In Shuttleworth's analysis of 2,380 cases the most prominent prenatal factor was a family history of tuberculosis (28.3 per cent.). Lapage considers that the influence of both tuberculosis and alcohol is small, but that the former has a little greater influence than the latter.

On the other hand, until recently, syphilis was held to be a very infrequent cause of the condition. From the results of the Wassermann reaction carried out by various observers within recent years it would appear that syphilis is a more frequent and potent cause than has hitherto been supposed from the purely clinical examination of the cases. Plaut emphasizes in cases where congenital syphilis is suspected the importance of examining serologically not only the patient but the parents and other members of the family. Lippmann in 78 cases of mental deficiency found that 9 per cent. gave a positive Wassermann reaction. Dean in 330 cases found 51 positive (15.4 per cent.). Fraser and Watson in 105 cases 51 positive

(48 5 per cent) Findlay and Robertson in 22 cases 13 positive (59 per cent) Thomsen Boas Hjort and Lechly in 2 061 cases 31 positive (1 5 per cent) If the cases where a positive result has been found in another member of the family be added the percentage is considerably increased even up to 70 per cent (Fraser and Watson)

Consanguinity of the parents is not a frequent cause though in such cases any morbid taint in the family would be much increased in the offspring Physical injury to the mother during pregnancy is much more likely to produce undesirable results than mental shock or strain the importance of which is much exaggerated more especially by the parents themselves At birth difficult labor with prolonged pressure on the head by forceps or otherwise may cause a secondary type of amentia from gross lesion of the brain Of the postnatal causes epilepsy and convulsions are less often a cause than an effect of an already present mental deficiency Infectious diseases in themselves cannot cause mental deficiency except by a toxic or inflammatory process acting on the brain though they may render an unsuspected case of mental deficiency more obvious Meningitis and encephalitis may be followed by permanent mental deficiency though in many such cases there is evidence of gross cerebral lesion such as hydrocephalus Permanent and complete deafness or blindness if proper education can be provided need not cause mental defect The mental defect associated with cretinism and certain nutritional diseases should as pointed out by Thomson be regarded rather as instances of acquired mental dullness than of true secondary amentia Injury in childhood may be followed by mental defect specially if the injury has been severe enough to produce a gross cerebral injury In the absence of gross disease its importance has been exaggerated

Diagnosis

The ease with which the diagnosis of mental deficiency can be confidently made depends on the age at which the patient is seen In young children the mental indications are few and indefinite Some of the well known types the mongol the cretin the hydrocephalic etc can be recognized at a glance Certain minor bodily deformities are frequently associated with mental deficiency such as general asymmetry and smallness of the head an epicanthic fold at the inner angle of the eye abnormalities of the palate and jaws malformations of the external ears and incurving of the little finger These so called stigmata of degeneration though not pathognomonic occur more frequently in the mentally deficient than in normal children and the association of two or more of these deformities

may be of some help in doubtful cases Frequently the first symptom which attracts the mother s attention is weakness of the back The child is late in learning to sit up and the head rolls feebly from side to side The half open mouth the big, lolling, protruded tongue the constant slavering the rolling nystagmoid restless movements of the eyes should give rise to suspicion The child may be unnaturally quiet making little or no noise save an ugly inarticulate sound and constantly repeating some senseless movement He makes little attempt to grasp things and fails to be attracted by bright and moving objects he is late in learning to recognize his mother or nurse In extreme cases he lies inert and motionless in his mother s arms taking not the least notice of his surroundings Control over voluntary movements is delayed He is late in learning to walk or talk and there is a certain awkwardness and clumsiness of all his movements In addition to being much delayed speech is imperfect and lalling is frequent As a general rule the later the child is in learning to walk and talk the more pronounced the mental defect Control over the bladder and rectum is slowly and imperfectly acquired complete control is often delayed till the child is seven or eight years of age Convulsive seizures are frequent and as already pointed out are more often a symptom than a cause of the mental deficiency In older children of school age the expression the gait and general bearing are often characteristic Careful questioning will give some idea of the powers of memory of attention and of association of ideas

Classification

There are two main groups of cases the primary or genetous (Ireland) including ninety per cent of all cases and the secondary *i e* consecutive to other diseases such as epilepsy meningitis syphilis etc It will be sufficient for our purpose to describe briefly certain of the most prominent and well known types

Primary Idiocy (or Amentia)

Simple Congenital Idiocy —There are no special physical characteristics The patients are undersized and less well developed physically than normal children the head is small and frequently asymmetrical A combination of two or three of the stigmata of degeneration is common The face is vacant with a dull stupid fatuous expression The features are often though not always coarse and heavy the mouth is half open with saliva dribbling from it In the young child the eyes wander aimlessly and are not attracted by bright and moving objects In older children there is a lack of coordination and their movements are awkward and clumsy They

are not good at games partly because of their lack of attention and partly because of the deficiency of coordination They walk with a shambling shuffling gait and when at rest the body is swung rhythmically to and fro in an aimless senseless sort of fashion Speech is often imperfect They cannot concentrate their attention on an object for any length of time and wander erratically from one object to another They have been well described as bird witted On the other hand it may be very difficult to attract their attention at all The power of memory is equally defective All degrees of mental impairment may be present from simple feeblemindedness to the lowest grades of idiocy In all in the higher grades no less than in the lower there is a characteristic lack of will power which renders them unusually susceptible to outside influences whether good or bad and this constitutes their chief danger from the social point of view and also one of the strongest arguments for their segregation in institutions under constant and efficient supervision Their emotions are little under control and violent and passionate outbursts are not uncommon In the severe degrees of idiocy the higher emotions are completely lacking

The Mongol—The mongolian type of idiocy was first described by Langdon Down in 1866 and was so called from the resemblance to the Kalmuc or Tartar type of feature The frequency of its occurrence among mental deficients is estimated by Shuttleworth at five per cent by Langdon Down at ten per cent and by Vogt at one per cent The most important etiological factor is that the majority of the cases are the last born of a large family and born at a time when the mother is approaching the climacteric Shuttleworth regards them as exhaustion products Sutherland calls attention to the frequency with which evidence of syphilis is found in these cases Stevens found the Wassermann reaction positive in the blood in two and in the cerebro spinal fluid in four out of twenty cases Pleocytosis was present in four and increase of globulin in eighteen

The cases have a curious family resemblance to each other The skull is rounded with a shortened anteroposterior diameter and the occipital protuberance is flattened so that the planes of the face and the occiput tend to be parallel The fontanelles and sutures are late in closing The hair is straight and sparse with a downy growth extending low on the forehead The face is rounded the palpebral fissures slope upwards and outwards epicanthic folds are frequent the bridge of the nose is broad and flattened the cheeks are full rounded and of good color the mouth is small and the lips everted and fissured and the tongue is constantly protruded After a time the papillae become enlarged and the tongue is scored with deep transverse fissures giving the characteristic hacked" tongue (lingua scrotalis) Though the child is undersized the limbs are well formed The hands are broad the fingers are short and the little finger

is stumpy and incurved towards the ring finger A wide cleft separates the big toe from the others Hypotonia of the limbs is well marked The re flexes as a rule are normal in a series of eight cases however Hill found an extensor plantar response in all Congenital cardiac defects are common Nystagmus squint and lens opacities as well as cataract are frequent (Pearce Rankine Ormond)

The mental defect may be of any degree As a rule the children are docile bright and tractable fond of music and unusually imitative

Post mortem the convolutions of the brain are found to be primitive and more simple than normal There are no constant microscopic changes

The prognosis is bad both from the mental and from the physical point of view and many of them succumb to tuberculous disease before the age of puberty

The Cretin —Cretinism or infantile myxedema is due to deficient or absent secretion of the thyroid gland Though the deficiency is present at birth, symptoms do not become manifest till the age of six or eight months The physical changes are characteristic The head is dolicho cephalic narrow in front and broad behind The child is squat and stumpy the features are heavy and ugly The hair is coarse and sparse like horse hair the forehead is low the eyes are set far apart the palpebral fissures are horizontal and narrowed from the subcutaneous infiltration the nose is broad and flat the lips are thick and everted the tongue is protruded from the half open mouth but is not fissured as in the Mongol The skin is coarse thick and dry the complexion yellowish or parchment like the expression dull and vacant

The myxedematous infiltration affects the subcutaneous tissues of the face as well as of the limbs and trunk Pads of fat occupy the supra clavicular regions the abdomen is distended and prominent the um bilicus tends to be everted and is often the site of a hernia The fingers are thick and broad the limbs short and stumpy The general metabolism is feeble the temperature is low and the child is sensitive to cold perspira tion is lacking the pulse is slow and constipation is common In the absence of thyroid *treatment both physical and mental* development remains in abeyance and the cretin of adult age retains the mental and physical characters of a child of four or five years old There is delay in learning to walk or speak and speech may be confined to the utterance of a few syllables The mental defect may amount to complete idiocy

The diagnosis is readily made as a rule though there may be some difficulty in distinguishing the cretin from the mongol The mental con dition of the achondroplasic is so totally different that confusion is not likely to arise

The Microcephalic —The microcephalic is readily distinguished by the

smallness and peculiar shape of the head The forehead is narrow the occiput flattened and the vertex high and pointed There are no special etiological factors save that the condition may occur in two or three members of a family The general hypoplasia of the brain leads to early closure of the fontanelles and not vice versa as had been at one time supposed In a child of school age the head should measure about nineteen inches in circumference but in the microcephalic it may not exceed fifteen to seventeen inches The size of the skull is out of proportion to the size of the face and the body generally Convulsions are common and some degree of spasticity, especially in the younger children is frequently present Like all mental defectives they are late in learning to walk and talk and to gain control over the bladder and rectum In disposition they are amiable and bright but liable to passionate outbursts The milder grades show considerable improvement under training and education

The Hydrocephalic—The mental deficiency associated with congenital hydrocephalus has already been referred to in the discussion of that subject

Tuberous Sclerosis—This is a rare developmental condition characterized by curious multiple neurogliomata in the brain sebaceous adenomata on the face and tumors elsewhere in the body Clinically there are convulsive seizures with progressive mental impairment

Secondary Amentia

The various types of secondary amentia have been differentiated largely on etiological grounds and it is usual to speak of the eclamptic the epileptic the traumatic the paralytic or diplegic the meningitic or postfebrile the syphilitic and lastly the amaurotic family idiocy (Tay Sachs disease)

The majority of mental deficients are liable to convulsive seizures whether the mental deficiency be a primary or a secondary condition Most often the seizures are an effect rather than a cause of the condition producing the mental impairment Many of the convulsive attacks of young children associated with other diseases (rickets digestive disturbances etc) or with the onset of an acute febrile illnes pass off without leaving any permanent mental damage In other cases there may be a single fit and from that time a progressive mental impairment sets in even though the fit may not be repeated In the cases where genuine epileptic seizures occur the prognosis is far from hopeful the fits are repeated and with the repetition a progressive mental enfeeblement occurs leading in many cases to complete dementia In children under the age of five or seven years epilepsy is almost invariably accompanied by mental degeneration

Any gross cerebral lesion causing paralysis is apt to be associated with mental weakness Spastic diplegia is the commonest form The cerebral

palsies of children may be due to malformation of the brain during intra uterine life to injury to the brain or meninges during prolonged or difficult labor or to conditions arising after birth The distribution of the paralyses may be hemiplegic paraplegic or monoplegic Associated with these is a varying amount of mental deficiency The mental weakness is apt to be overestimated in these cases owing to the paralysis which renders the children even more helpless than usual Many of them have a considerable degree of intelligence and are capable of education and mental development the prognosis being more hopeful than many of the types already described

Cerebrospinal meningitis polioencephalitis and other toxic or inflamma tory processes affecting the brain in children are frequently followed by a considerable degree of mental deficiency the degree depending on the sever ity of the original inflammation These causes may act by producing sense-deprivation leading to permanent and complete deafness or blindness or by producing sclerosis and scarring in the brain itself In the first of these conditions the child s mental development is arrested and in time he becomes mentally backward though this is not necessarily permanent provided that suitable educational methods are available, in the second group of cases the child becomes and remains a mental deficient the brain matter itself having been permanently damaged or destroyed Meningitis is not a frequent cause of mental deficiency in children though many of the congenital types are believed by some alienists to be due to intra uterine inflammatory processes of the brain or meninges

The increasing importance of syphilis as an etiological factor has already been referred to One of the most important varieties of syphilitic affection is the adolescent or juvenile general paralysis which occurs in congenital syphilitics about the age of puberty Dementia and paralysis occur early and lead within a short time to a fatal termination Thomson calls atten tion to a form of hydrocephalus of syphilitic origin which is not infrequent

Amaurotic Family Idiocy (Tay Sachs Disease)

This is a family disease occurring exclusively among Jews Its etiology is quite unknown but syphilis is said not to be a factor The children are born healthy but within a few months they show a progressive mental deteri oration failure of vision and paralysis affecting the greater part of the body The child is unable to hold up the head the limbs are flaccid rarely spastic The reflexes may be normal diminished or exaggerated Examination of the ocular fundi shows a typical cherry red spot at the macula The condition passes on to complete blindness with simple optic atrophy and the child dies in a marasmic state before the age of two years

TREATMENT

In the treatment of the mentally deficient it should be kept in mind that the condition is a lifelong one and incurable but even so in the majority of cases the time spent on training and education is well worth while Though no great mental development may be possible all except the lowest grades of idiot can be taught habits of personal cleanliness orderliness and decency and many may learn some simple manual occupation the performance of which will occupy all their energies and help to keep them happy and contented

They are underdeveloped in body as well as in mind and medical treatment is carried out on general lines *e g* by the provision of abundant nourishing easily digested food suitable exercise warm clothing fresh air and simple tonics such as iron cod liver oil and malt in the more debilitated cases Special conditions (*e g* thyroid insufficiency epilepsy syphilis *and tuberculosis) should be treated with appropriate remedies Refractive* errors defective teeth enlarged tonsil and adenoids otitis media and deafness contracted tendons etc should be rectified

The parents of the mentally deficient child are rarely the most suitable persons to undertake his treatment and training and most of these children will be happier and will make more progress in an institution specially devoted to the care of such cases For the details of the special methods adopted the reader is referred to the special article of Miss Dendy in Lapage's book on Feeblemindedness in Children of School Age

BIBLIOGRAPHY

DENDY M *Feeblemindedness in Children of School Age* Appendix 1 Lapage C P Manchester 1911
DEAN H R Proc Roy Soc Med Lond 1910 III Pt 2 Neurolog Sect 117
DOWN J L H Clin Lect and Report Lond Hosp Lond 1866 III 259
FINDLAY L and ROBERTSON M E Glasgow M Jour 1914 LXXXII 401
FRASER K and WATSON H F Jour Ment Sc Lond 1913 LIX 640
GOODALL E Lancet Lond 1914 II 1457
HILL W B *Quart J Med* Oxford 1908–09 II 49
IRELAND W W The Mental Affections of Children 2nd ed Lond 1900
LAPAGE C P Feeblemindedness in Children of School Age Publications University Manchester Med Series XIII Manchester 1911
LIPPMANN H Munchen med Wchnschr 1909 LVI 2457
PLAUT Cited Syphilis and the Nervous System Nonne Translat by Ball 2nd ed 1916 343

PEARCE F H RANKINE R and ORMOND A W Brit M Jour Lond 1910 II 186
Report of the Royal Commission on the Care and Control of the Feebleminded London 1908
SACHS B Osler and McCrae System of Medicine Phila and N Y 1910 VII 368
SHUTTLEWORTH G F and BEACH F Allbutt and Rolleston System of Medicine Lond 1910 VIII 874
SHUTTLEWORTH G E Brit M Jour Lond 1910 II 661
STEVENS H C Jour Am M Ass Chicago 1915 LXIV 1636
SUTHERLAND G A Practitioner Lond 1899 LXIII 632
THOMSEN O BOAS H HJORT R and LESCHLY W Berl klin Wchnschr 1911 XLVIII 891
THOMSON J Garrod A F Batten F I and Thursfield H Diseases of Children Lond 1913 868
TREDGOLD A F Mental Deficiency London 1908
VOGT H Ztschr f d Erforsch u Behandl d jugendl Schwachsinns Jena 1906–07 I 445

CHAPTER X

APHASIA

By J. M. Nielsen

Table of Contents

Historical

In the beginning of the nineteenth century the subject of cortical localization of cerebral functions, so important in aphasia, did not exist. The opinion and teaching of Flourens were accepted universally, that in case of injury or disease one part of the brain could substitute for another. When the concept of cerebral localization did arise, unfortunately it came in the form of the now disreputable phrenology. Gall was the originator of that pseudo-science which still is nursed by certain cultists of today. Gall himself, however, knew a great deal of anatomy, much more than some others of his day; he merely misapplied it in phrenology.

The first to correlate scientific observation with the concepts of cerebral localization was the Englishman Marc Dax, who noted that when hemiplegia was associated with disturbance of speech, it was nearly always a right and not a left hemiplegia However while Dax discussed his ideas he did not publish them for which reason the Frenchman Bouillaud[1] became the first to place on record the results of autopsy observations in what is now known as aphasia When he did so he drew conclusions which differed from those of Dax in that he located the faculty of speech in the frontal lobes without regard to laterality Eleven years after Bouillaud s contribution Dax published the results of his observations He had not changed his views but still believed that the left side of the brain contained the anatomical structures on which language was based

Bouillaud continued his researches and promulgated his views but he was opposed by Cruveilhier and by Paul Broca After much discussion a patient was studied jointly by Bouillaud and Broca, and it was agreed that autopsy should settle the issue The case came to autopsy Bouillaud was correct, and Broca was converted to the doctrine of cerebral localization

Then Broca proceeded independently and in 1861[3] presented his now famous report of two cases to show that the faculty of articulated language was located not only in the frontal lobes but *at the foot of the third left frontal convolution* The report was the more startling because in both cases the lesions were large and it was only by deduction that he arrived at the exact site which he named In one case the brain was not even sectioned but was preserved uncut as a museum specimen Broca termed the loss of the faculty of articulated language aphemie (aphemia)

Trousseau[4] in close association with Broca at first followed Broca's teachings but departed from their narrow confines because of certain conflicting cases He also suggested the word *aphasia* to replace Broca s aphemia when he learned that in Greek aphemia meant infamy while aphasia meant speechlessness Broca accepted Trousseau s new term aphasia and it has become so firmly rooted that undoubtedly it will remain in spite of the marked changes in modern concepts

Wyllie an Englishman in 1866 distinguished between motor and sensory aphasia He said that " word ideas of associated motions which form the faculties of speech are supra motory while the situation of associated sensations which form the faculty of word comprehension is supra sensory ' Moxon, another Englishman suggested the first principles of apraxia when he stated that the centers for movement which were located on the left side of the brain had a governing influence over the similar centers of the right side In 1867 William Ogle suggested the term *agraphia*

During this period one of the greatest scientific figures of all time arose in England John Hughlings Jackson He was so far above his contemporaries in depth

of thought in power of analysis and in foresight that like other prophets ahead of their time he was not appreciated It was Arnold Pick of the German University of Prague an excellent linguist who pointed out the great value of Jackson s work In the subject of what is now known by the broad term of aphasia Jackson s contributions included the concept that the right side of the brain was not passive in language but that it could perform to some extent after the left was out of function He also reported the first case of visual agnosia for objects under the title of imperception and he pointed out that patients with motor aphasia were often unable to protrude the tongue apraxia of the mouth

In 1874 Wernicke[7] *of Breslau a young man of 26 years published a remark*able monograph Der aphasische Symptomencomplex in which he delineated sensory aphasia much as Wyllie had done but surpassed Wyllie by presenting a series of cases with autopsy findings Since his day lack of comprehension of spoken language with alexia and agraphia has been known as Wernicke s aphasia In view of the pioneer character of his work it is entirely pardonable that he made a few errors Patients with sensory aphasia he believed failed to comprehend spoken language because they failed to hear the words It is well known now that one hears equally well with both temporal lobes in Wernicke s aphasia patients fail to recognize the words They cannot read or write because of loss of recognition of the words which are a necessary prerequisite for comprehension

In 1885 Kussmaul published an excellent monograph on aphasia in which he standardized nomenclature He also pointed out some of the errors which Wernicke had made and on the whole considerably advanced the subject

The concept of psychic blindness now called visual agnosia for objects came prominently to the fore at this time due to pioneer work of Munk and Hitzig in Germany and of Luciani and Seppilli in Italy Charcot in France and Wilbrand in Germany made clinical application of this experimental work on animals Charcot next applied his concept of mind blindness to symbols and correctly postulated that a lesion of the angular gyrus was the cause of alexia (It is not the only possible cause however)

After Wernicke s work had been established Lichtheim appeared as an enthusiastic follower of Wernicke and the two labored in close association Diagrams were made of isolated centers with lines connecting them and attempts were made to force clinical pictures into the diagrams Some authors inserted a concept center while others denied such a structure Some explained clinical pictures on the basis of lesions in centers others on the basis of lesions between them Still others saw undescribed possibilities in the diagrams and predicted syndromes before they appeared When these syndromes then were seen such an occurrence ' proved the correctness of the diagrams This age is now referred to as the age of diagram makers and we smile at the naivete of the designers yet it is only

in the last decade that some of the points which confused those students have become clear

The concept of isolated centers took so firm a hold on students of aphasia that it was thought possible to explain every symptom on the basis of a focal lesion When this system failed correctly to predict autopsy findings, Freud[7] in 1891 produced a long article to show that all aphasia was conduction aphasia Thus the pendulum swung in both directions However, Freud made one valuable suggestion which was immediately accepted he introduced the term, *agnosia* to designate loss of power of recognition Dejerine[1] declared against autonomy of the centers, and M Allen Starr[11] of our own country reported that he had failed to find any case substantiating Broca s concept of aphasia Charles K Mills[1] favored the localization doctrine and became the leader of thought in that direction in America

In 1906, when the moment was right for any sort of radical dissension, Pierre Marie came forth with the radical statement that the third left frontal convolution played no essential role in aphasia that there was only one type of aphasia, Wernicke's aphasia, and that Broca's aphasia was Wernicke s aphasia plus anarthria However, he redefined anarthria stating in so many words that it was equivalent to the classical subcortical motor aphasia " (The classical subcortical motor aphasia was a syndrome of total inability to speak with completely intact control of tongue and mouth) Examination of his thesis[13] shows that he arrived at his peculiar conclusion by also redefining the term aphasia He wrote (page 16), " D apres ce que nous avons dit plus haut de caracteres de l aphasie de Broca et de l aphasie de Wernicke, on voit que ce qui au point de vue d une saine classification nosologique doit constituer en somme *l aphasie vraie* ce n est pas le fait de parler mal ou de ne pas parler du tout ce qui constitue l aphasie, c est le fait de comprendre insuffisamment le parole de presenter cette decheance intellectuelle particuliere sur laquelle nous avons insiste dans le premiere partie de cet article et enfin fait tres important d avoir perdue la faculte de lire et d ecrire ' Thus, speaking poorly or not speaking at all was not aphasia as it had been from its inception and still was to all students of the subject, but loss of ability to understand to read and to write was ' true aphasia

To make matters worse in 1908 Moutier[14] a pupil of Marie, at his master s instigation published a large monograph to prove the correctness of their views He gathered a mass of clinical and pathological material and a noble bibliography He cited cases which in other hands would have proved Broca correct, but with true loyalty to his master he ignored the contradictory data and enhanced the cases which could be interpreted as favoring Marie After the year 1908 the subject remained badly disorganized

In the meantime another historical figure appeared in the person of H Liep

mann[15], who made an epochal contribution to the subject of *apraxia* Prior to Liepmann it was thought that loss of ability to use the limbs correctly to a pur pose in the absence of ataxia paralysis chorea or ' mental causes was due to loss of recognition of the purpose Liepmann however studied a case of unilat eral apraxia in which the patient used his left limbs correctly but could not use his right though well innervated ones to an intelligent purpose When he used his right limbs, he appeared demented e g he would pour water on his head instead of into a glass but with the left ones he acted normally Apraxia was therefore proved to be a motor deficiency phenomenon

When apraxia was correctly recognized French writers especially Laignel Levastine Foix and Claude saw that motor aphasia was a type of apraxia

While all this work on cerebral localization of agnosia apraxia and aphasia was in progress workers in the field of psychology were by no means idle Hugh lings Jackson and later Head[1] in England did enormous amounts of work Head set aside all that was known about aphasia and starting anew brought forth a new terminology

In view of the complete disorganization of the subject Head s attitude was well justified In fact as late as 19 6 S A K Wilson stated that not only was aphasia not understood but the approach to be adopted was not agreed upon The weakness in Head s work was that it was not and could not be based upon anatomy and physiology Pick in the German University of Prague and Kurt Goldstein in Germany adopted the psychological approach Charcot[17] an other wise arden localizationist took the psychological approach in one sense he con sidered some persons visual minded others auditory minded and thought that different persons reacted differently after identical lesions Wilson wrote an excellent little monograph in 1926 which showed a clear orientation He pointed out the inconsistency in combining anatomical physiological and psychological concepts and terms in a single approach

In 1920– 2 the most remarkable work ever published on the subject of aphasia appeared from the pen of Henschen[1] in Uppsala Sweden By an appeal to authorities in various countries he caused to be gathered every case of aphasia in the world literature with autopsy findings and many additional clinical ones All cases were abstracted in the original language of the author except that Rus sian and Scandinavian cases were rendered in German After a meticulous analysis incontrovertible proof of many facts was established He showed that anatomy and physiology were sufficient to explain all facts of aphasia agnosia and apraxia He also showed that different individuals were differently endowed and trained and that the statistical approach was necessary for a complete under standing of the subject He showed that some persons were able to train the right side of the brain in language after destruction of the language area on the left

side, while others were unable to do so He established the average and the exceptional and above all proved that it was well worth while to train an aphasic by education of the corresponding homologous area of the minor side

Unfortunately the work of Henschen, because of its voluminous size and its rendition in four languages, was read relatively little Weisenburg and McBride produced their monograph after Henschen's work and arrived at the conclusion that the brain functions as a whole in language" On the other hand Potzl[6] in Vienna recognized all the anatomico physiological facts and proceeded as Hen schen had done Kleist[1] followed suit on the war injuries of World War I In 1936 Nielsen and FitzGibbon published a small monograph giving full value to Henschen s and to Potzl s work The work was essentially an epitome but it resulted in the fairly general acceptance of the classical doctrine of aphasia Nielsen later corrected and added details on the basis of further observations in a textbook of neurology Stanley Cobb[3] has accepted the viewpoint and has made valuable contributions to its dissemination

From 1935 onward neurosurgery made possible a series of crucial cases of unquestionable focal lesions through the art of lobectomy It became obvious that, when a major temporal lobe was removed, the patient still could comprehend spoken language slightly and that such comprehension took place through the function of the minor temporal lobe It also became obvious that any surgical procedure in the frontal lobe impinging on Broca s convolution resulted in aphasia The results of occipital lobectomy were established and even an occa sional case of removal of the angular gyrus was reported (Raney)

The Nature of the Evidence

Humanly designed experimental work in the sphere of language is impossible because only human beings have the function in the sense here considered The only approach therefore is the clinico pathological one Nature undoubtedly provides all of the material necessary for the complete solution of the problem of aphasia in a single year but it is discarded by doctors who are not research minded and by practicing cultists It is not enough to make observations the facts must be publicized if the profession is to have them for public good Probably not more than one one hundredth of one per cent of human illness is sufficiently studied followed by scientific examination of the evidence and published In aphasia 125 years were required for the entire literature of the world to provide the answer as we now have it There are still a few unknown items

For detailed publication elsewhere the writer has gathered 18 cases of hemispherectomy i e cases in which the major language area or hemisphere had either been removed surgically or destroyed by disease In those 18 cases com

prehension of spoken language was recovered to a state which could be called excellent in 2 good in fair in 4 slight in 6 practically nil in 4 Spontaneous speech became excellent in 1 fair in 3 slight in 11 remained nil in 3 Recovery of the functions of reading and writing was exceptional Since the major speech area was destroyed there can be no question that the minor side performed the language function of which the patients became capable

Next 44 cases were gathered in which Broca s convolution or a little additional tissue was destroyed Recovery of spoken language was almost nil in 25 but fair to good in 19 Thus some persons can train the minor area of Broca while others can not When the cases were selected more strictly to segregate those with small lesions restricted to Broca s convolution the result was the same so far as emissive speech was concerned as though hemispherectomy had been performed As Broca s convolution must therefore contain the engrams of motor speech one need not be so careful about the size of the lesions the additional destruction does not affect capacity for emissive speech The cases of lesions not restricted to Broca s area were utilized only if recovery had been good

Twelve cases of destruction of the major temporal lobe were gathered mostly from the Los Angeles General Hospital These cases were analyzed and it was found that they showed loss of comprehension of spoken language of language formulation and of ability to read and to write Emissive speech also was lost to some degree as would be expected since the minor language area was compelled to formulate the language to be emitted Such is the nature of the evidence upon which the following description is based The work of a century is now to be epitomized

Agnosias Apraxias and Aphasias

The agnosias apraxias and aphasias are understood only by a consideration of the normal cerebral physiology as related to recognition associative motor functions and language This is due to the fact that the three conditions are merely deficiency syndromes of which eugnosia eupraxia and euphasia are the normal counterparts

The cerebral cortical connections are divisible into two great categories the projection fiber systems and the association systems Among the former are the pyramidal tracts the thalamocortical bundles and the auditory and visual pathways The association systems associate various portions of the cortex with each other they are much more numerous and complex than the projection fiber systems

For many years neurologists thought of the various cortical centers as being either sensory or motor It must be obvious however to the student who ponders the subject that all so-called cerebration takes place in the engrams between

the sensory and the motor and that the fibers subserving the complicated cerebral mechanisms of thought are association systems *All agnosias, apraxias and aphasias result from disturbance of the association and not of the projection fiber systems* The physiology of the association systems will be considered so far as it is essential to an understanding of the subject at hand

Definitions

Agnosia was a term suggested by Freud to replace Finkelnburg s asymbolia He stated that asymbolia was more appropriate for the relation between word and object concept than it was for the relation between object and object concept This differentiation is not clear, unless one has thought a great deal about the matter In his summary of the subject he stated more simply that he suggested *agnosia* for *loss of recognition of objects* It was understood that primary perception must be intact and that general mental function must be sufficient for recognition Even with these explanations however, the definition, as he gave it, proved too simple It soon became evident that agnosia must have a qualifying adjective to indicate the sense organ through which recognition is no longer possible Thus one may have visual agnosia, auditory agnosia or tactile agnosia (astereognosis) Gustatory and olfactory agnosias still are unknown A person may have more than one agnosia at one time, but if so, the fact must be stated

A corollary came into being very soon If loss of visual recognition of objects was visual agnosia for objects then loss of recognition of symbols must be agnosia for symbols Hence visual verbal agnosia auditory verbal agnosia and similar designations for mathematical figures and for musical symbols etc became accepted terms The agnosias concerned with symbols are part of aphasia as will be clear when the definition of aphasia is given Briefly stated then *agnosia is loss of recognition of objects, pictures or symbols through one sense organ sufficient primary perception and adequate general mentation being presupposed*

Apraxia is an old term which has changed markedly since its inception Until the time of Liepmann 1900–1906 one spoke of motor apraxia and sensory apraxia and the term was for a time synonymous with asymbolia It is now generally agreed that *apraxia is a disturbance of motor function due to an organic lesion of the association systems of the brain* It is presupposed that paralysis, ataxia asynergia and general mental disturbances are excluded as causes

Aphasia as stated in the historical review first was understood as speechlessness When sensory aphasia was discovered a new name was not chosen the well established aphasia was recognized as having two forms Then many more forms were discovered and it became clear that a very broad definition was in order *Aphasia became defined as any disturbance of symbolization by means*

of which man communicates in thought with his peers Again sufficient general cerebration is presupposed and the causative agent must be an organic lesion It will be clear that agnosia for objects is not aphasia but that *all agnosias for symbols are part of aphasia* Furthermore apraxia of speech is identical with motor aphasia Aphasia includes all forms of acquired alexia and agraphia regardless of where the rupture of the physiological (cerebral) chain may have occurred

It would be quite a simplification and therefore an improvement to restrict the use of the term aphasia to mean the language component of We could thus avoid duplication as at present when a certain defect is both an agnosia and an aphasia or an apraxia and an aphasia However this is not the place to agitate for reforms but simply to record the facts using the generally accepted nomenclature

In the discussion to be presented the physiological plan is followed from the simplest function in each instance to the most complex

THE AGNOSIAS

Visual Object Agnosias

There are three levels of visual cortical integration primary or perception (also called primary perception) secondary or recognition and tertiary or revisualization The first function is performed by area 17 of Brodmann on the borders of the calcarine fissure Of the calcarine area the pole is concerned with macular vision while the remainder subserves the periphery of the retina This fact is of some importance in agnosia because inasmuch as the periphery of the retina serves chiefly for perception of *motion* and the macula for *accurate observation of still objects* it is mainly the occipital poles which are of importance in recognition and consequently in agnosias In our scheme of the pathways followed in visual recognition the pole is the essential portion of the cortex to be considered With these fundamental facts before us we shall dismiss consideration of the primary visual cortex because all of the visual agnosias are caused by lesions of the secondary visual cortex or its subcortical fibers

By reference to the illustration of Brodmann s cytoarchitectonic areas it is seen that area 18 is immediately adjacent to area 17 It is the portion of cerebral cortex essential to *recognition* of objects and pictures The physiology of such recognition is as follows The first time that an individual perceives an object (with area 17) a set of impulses goes to area 18 where an engram representative of the object is formed By that statement is meant that the impulses travel over a set of neurons and leave an imprint on them an imprint which is the

the sensory and the motor and that the fibers subserving the complicated cerebral mechanisms of thought are association systems *All agnosias apraxias and aphasias result from disturbance of the association and not of the projection fiber systems* The physiology of the association systems will be considered so far as it is essential to an understanding of the subject at hand

Definitions

Agnosia was a term suggested by Freud to replace Finkelnburg s asymbolia He stated that asymbolia was more appropriate for the relation between word and object concept than it was for the relation between object and object-concept This differentiation is not clear, unless one has thought a great deal about the matter In his summary of the subject he stated more simply that he suggested *agnosia* for *loss of recognition of objects* It was understood that primary perception must be intact and that general mental function must be sufficient for recognition Even with these explanations however, the definition, as he gave it proved too simple It soon became evident that agnosia must have a qualifying adjective to indicate the sense organ through which recognition is no longer possible Thus one may have visual agnosia, auditory agnosia or tactile agnosia (astereognosis) Gustatory and olfactory agnosias still are unknown A person may have more than one agnosia at one time, but if so, the fact must be stated

A corollary came into being very soon If loss of visual recognition of objects was visual agnosia for objects then loss of recognition of symbols must be agnosia for symbols Hence visual verbal agnosia auditory verbal agnosia and similar designations for mathematical figures and for musical symbols, etc , became accepted terms The agnosias concerned with symbols are part of aphasia as will be clear when the definition of aphasia is given Briefly stated, then, *agnosia is loss of recognition of objects pictures or symbols through one sense organ, sufficient primary perception and adequate general mentation being presupposed*

Apraxia is an old term which has changed markedly since its inception Until the time of Liepmann, 1900–1906, one spoke of motor apraxia and sensory apraxia and the term was for a time synonymous with asymbolia It is now generally agreed that *apraxia is a disturbance of motor function due to an organic lesion of the association systems of the brain* It is presupposed that paralysis, ataxia, asynergia and general mental disturbances are excluded as causes

Aphasia as stated in the historical review, first was understood as speechlessness When sensory aphasia was discovered a new name was not chosen the well established aphasia was recognized as having two forms Then many more forms were discovered, and it became clear that a very broad definition was in order *Aphasia became defined as any disturbance of symbolization by means*

of which man communicates in thought with his peers Again sufficient general cerebration is presupposed and the causative agent must be an organic lesion It will be clear that agnosia for objects is not aphasia but that *all agnosias for symbols are part of aphasia* Furthermore apraxia of speech is identical with motor aphasia Aphasia includes all forms of acquired alexia and agraphia regardless of where the rupture of the physiological (cerebral) chain may have occurred

It would be quite a simplification and therefore an improvement to restrict the use of the term aphasia to mean the language component of We could thus avoid duplication as at present when a certain defect is both an agnosia and an aphasia or an apraxia and an aphasia However this is not the place to agitate for reforms but simply to record the facts using the generally accepted nomenclature

In the discussion to be presented the physiological plan is followed from the simplest function in each instance to the most complex

THE AGNOSIAS

Visual Object Agnosias

There are three levels of visual cortical integration primary or perception (also called primary perception) secondary or recognition and tertiary or revisualization The first function is performed by area 17 of Brodmann on the borders of the calcarine fissure Of the calcarine area the pole is concerned with macular vision while the remainder subserves the periphery of the retina This fact is of some importance in agnosia because inasmuch as the periphery of the retina serves chiefly for perception of *motion* and the macula for *accurate observation of still objects* it is mainly the occipital poles which are of importance in recognition and consequently in agnosias In our scheme of the pathways followed in visual recognition the pole is the essential portion of the cortex to be considered With these fundamental facts before us we shall dismiss consideration of the primary visual cortex because all of the visual agnosias are caused by lesions of the secondary visual cortex or its subcortical fibers

By reference to the illustration of Brodmann s cytoarchitectonic areas it is seen that area 18 is immediately adjacent to area 17 It is the portion of cerebral cortex essential to *recognition* of objects and pictures The physiology of such recognition is as follows The first time that an individual perceives an object (with area 17) a set of impulses goes to area 18 where an engram representative of the object is formed By that statement is meant that the impulses travel over a set of neurons and leave an imprint on them an imprint which is the

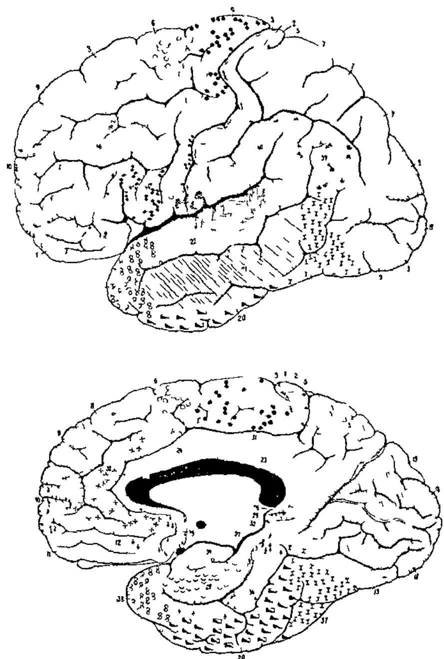


FIG 1 — Brodmann's cytoarchitectonic areas Of particular importance in aphasia are area 44 Broca convolution areas 41 and 42 Wernicke's area 39 the angular gyrus 37 language formulation area and the occipital areas 18 and 19 for recognition and revisualization respectively

anatomical basis of the memory of the seeing When the same object is seen the second time the impulses travel over the same pathway again now the object is recognized For as long as the memory lasts whenever an identical article is perceived the engram is found to be already recorded and hence the object is recognized as being identical Area 18 thus serves as a card index for area 17 in the sense that only area 17 can consult it nothing can be recognized that is not first seen

In the average human being all engrams of objects in area 18 are made and trained bilaterally a lesion of the cortex or subcortex of one side does not cause visual agnosia for objects In exceptional instances however the individual trains only one side and that side is not necessarily ipsilateral to the major language area Besides some exceptional persons will train one side for recognition of animate objects while training the other for recognition of inanimate ones

A patient suffering with visual agnosia for all objects is lost in familiar surroundings Everything he looks at seems like something new seen for the first time If the lesion is bilateral he cannot recover because he has no area to train everything continues to look strange even though he may look at it often He avoids objects in his path and obviously sees (perceives) but he must utilize his other senses to recognize anything He identifies a watch by its tick an orange by its smell or taste a knife by touch etc

There is a great deal of evidence that in most persons area 18 is divided by a horizontal line into an upper area for recognition of animate objects and a lower for inanimate objects Thrombosis of the posterior cerebral artery of the major side in a number of instances has caused visual agnosia for inanimate objects while recognition of animate ones was preserved And the writer has reported cases of the opposite kind from proved lesions of the upper portion (autotopagnosia) A considerable number of cases have been reported in which certain attributes of objects have been lost separately We thus have visual agnosia for form size direction (geometric optic agnosia) color (achromatopsia or hemiachromatopsia as the case may be) or for the body or its parts (visual finger agnosia or confusion of laterality)

Olsen has reported a case in which agnosia for objects of all kinds was complete *except for color* The writer studied the case with him and found that the patient named the color of every object shown to her without having the slightest idea of what the object was Others have reported similar cases Achromatopsia is however far more common

One of my patients (C H C) suffered first a thrombosis of a portion of the left middle cerebral artery which produced amnesic aphasia Months later he suffered a small thrombosis in the right area 18 verified at autopsy After the second lesion he recognized animate objects and knew his nurses doctors and all visitors

but he failed to recognize his food, the mountains, the grass, automobiles and all other inanimate objects He recognized flowers, the only case on record in which this distinction has been made He looked out of his hospital window, pointed to the mountains and automobiles and asked what " those things ' were He would not accept any food offered by his nurses, unless they named each spoonful for him, but when he looked out and saw a mule grazing, he said, ' Look at that mule eating '

Another patient of the writer with a lesion located parasagittally in the left occipital lobe, shown at autopsy, failed to recognize any animate object, and she included in that category a set of artificial teeth When shown a group of objects including a pen knife, key, bill fold, pencil, pen a set of teeth, various coins and a safety pin she selected any object on request except the teeth When they were left alone and she was asked to pick up the teeth she replied, ' There aren t any teeth " When shown a hand, she did not recognize it, and when shown a doll, she named the color and the clothing but did not know the object This was a case of generalized visual autotopagnosia

Loss of the sense of direction is variously named according to whether the patient is disoriented relative to the cardinal points (disorientation in space) and sees direction of lines clearly, or whether he remains oriented himself and sees faulty direction in lines (geometric optic agnosia)

Wolpert has described a condition which he called simultanagnosia, characterized by inability to synthesize the elements of a picture into a concept of action The patient sees horses and riders but not the race The condition is wrongly named as it is a disturbance of concept formation and not agnosia The causative lesion is in the major occipital lobe

One patient of the writer after a cerebral vascular lesion and right homonymous hemianopia could not find his way about in his familiar neighborhood The streets ran in bizarre directions and he could not find the ocean, which was due west a quarter of a mile Neither could he find his way about his house, but he recognized the objects in his home and the buildings which he had known

A nurse aged 49 years after a cerebral lesion asked when the other nurses had taken to wearing black instead of white uniforms She could not recognize a teapot a cup or an orange by sight Yet she identified all objects by touch, taste or smell and a watch by the tick After two years she had learned to recognize all such objects by sight having trained herself by outlining them in the air with her fingers

In 1924 Gerstmann reported a new syndrome of what he called finger agnosia confusion of laterality acalculia and agraphia He showed the causative lesion to be located at the posterior border of the angular gyrus encroaching on that gyrus and area 19 of Brodmann Through numerous studies by many investi

gators it has been shown conclusively that all of the elements of the Gerstmann syndrome may occur separately and that a relatively large lesion is necessary to cause all of them I have shown already that generalized autotopagnosia may result from a focal lesion of the occipital lobe What Gerstmann called finger agnosia was visual finger agnosia apractic failure to demonstrate the fingers and tactile finger agnosia As cautioned above it is necessary to relate any agnosia to one sense organ only and if there are several simultaneous agnosias the fact should be stated

Visual Symbol Agnosias

In the realm of recognition of symbols there are of course the same two levels of physiological function as in recognition of objects one for primary perception (identical with that for objects) area 17 and a second for recognition namely the angular gyrus area 39 of Brodmann The angular gyrus thus serves in recognition of symbols as area 18 does in recognition of objects There is this important difference between them physiologically that while there is usually little tendency to train area 18 on one side only there is a strong inclination to train only one angular gyrus This fact clearly seems based on the unilaterality of training in the entire sphere of language

In the angular gyrus of the major side are stored engrams of recognition of letters words and musical symbols Mathematical symbols apparently are stored at the upper border of the angular gyrus on the borders of the interparietal sulcus It will be shown later that the engrams of recall of symbols also are stored in the angular gyrus but this fact is not related to agnosia

A lesion destroying the cortex of the major angular gyrus causes loss of ability of the patient to recognize symbols by vision alone If the angular gyrus is separated from the occipital pole by a subcortical lesion the patient will likewise lose ability to recognize symbols The symptom is known as visual verbal agnosia visual literal agnosia visual musical agnosia or visual agnosia for mathematical figures as the case may be Unless there is some other lesion as well the patient will be able to read embossed letters and words by touch He will even be able to read written and printed words by tracing them with his finger as the 40 year old nurse mentioned above was able to do

Auditory Agnosias

The cortical area for primary perception of sounds is in area 52 of Brodmann the transverse temporal gyri chiefly the first of each side Where these gyri terminate laterally by merging with the superior temporal convolutions are found

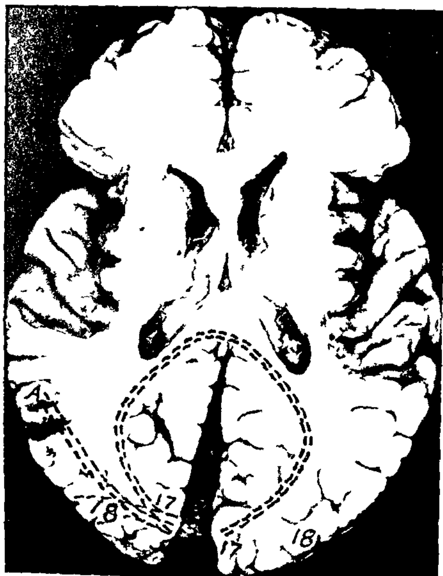


Fig 2 — Diagram on a dissected specimen of the simplest possible pathways for impulses in recognition of objects and symbols The occipital pole part of area 17 is used for *perception of still objects* Area 18 of one or both sides is used for *recognition of objects* and area 39 the angular gyrus marked A for *symbols* The transverse gyri of Heschl have been exposed by removal of the operculum

areas 41 and 42, commonly known as Wernicke's area These areas are roughly semicircular as seen on the lateral surface of the brain they are essential to *recognition* of sounds and hence are comparable to areas 18 for vision except that

they also serve for symbols Destruction of the areas of Wernicke renders the patient totally agnostic for sounds except music i e he does not remember ever having heard sounds other than musical ones before Engrams of language sounds are trained only crudely on the minor side for which reason destruction of the major one only leaves little function in recognition of language But for sounds other than symbolic sounds of whistles automobile horns watch tick crumpling of paper etc and for music the minor functions quite well

Destruction of the area of Wernicke of the major side leaves the patient unable to recognize spoken language he has auditory verbal agnosia except for the little recognition mediated by the minor side

The cortical area for recognition of music is at the anterior extremity of the superior temporal convolution area 38 of Brodmann The engrams of area 38 usually are trained very well on both sides for which rea on a lesion of either side leaves the patient able to recognize music about as well as ever However de truc tion of both sides renders him unable to recognize music at all

Tactile Agnosia (Astereognosis)

The physiology of touch differs from that of vision and of hearing in that the thalamic station serves for recognition of the sensation While the lateral geniculate body is an end station for vision and the median geniculate body serves similarly for hearing these thalamic nuclei do not convey impulses into consciousness in man But the thalamic nuclei for general sensation do suffice in man for recognition of the sensation they merely do not render localization possible For accurate localization of general sensation in man the post central gyrus is essential That gyrus and a portion of the superior parietal convolution serve for recognition of sensations, and a lesion of those areas causes tactile agnosia in the opposite limbs There is no major or exclusive training of one side each side serves for the opposite limbs, chiefly the hands

Gustatory and Olfactory Agnosias

These agnosias are not sufficiently e tablished in man to render intelligent dis cu sion possible Henschen has reported a case which he considered one of gustatory agno ia but no others have ever been claimed definitely

CORTICAL MOTOR PATTERN APRAXIAS
(KINETIC APRAXIA OF THE LIMB LIEPMANN)

In the preceding pre entation of the agnosias sensory elaboration of perception in the realm of the special senses was carried as far centralward as it could

be carried without entering the field of concept formation The next step would have entailed a description of concepts In the presentation immediately to follow the physiology of the motor mechanism is to be given below the physiological level of motor planning Motor planning itself involves a description of concept formation

Assuming now that a motor plan has been made, the physiology of its execution does not begin with stimulation of the Betz cells their function is not coordination of stimuli into movement but only that of causing impulses to travel down the pyramidal tract If a purposeful coordinated movement is desired the proper combination of cells in the precentral gyrus must be selected, and this selection is made by another set of neurons also located in the precentral gyrus apparently just anterior to the projection cells furnishing axons to make up the pyramidal tract A disturbance of these patterns causes the simplest form of apraxia, which Liepmann called kinetic apraxia of the limb I have called it *cortical motor pattern apraxia,* because it affects in some instances apraxia of swallowing apraxia of lip movement, apraxia of eyelid closure, etc in addition to limb apraxia Apraxia of swallowing has been reported from lesions in the pararolandic opercular cortex

A woman was referred to the writer for psychotherapy because of paralysis of the right arm which hung dangling like a flail and a diagnosis of hysterical paralysis had been made Examination showed the limb could be moved as a whole, but that individual finger movement was impossible, and that the deep reflexes of the limb were increased On that basis the diagnosis was changed to a lesion of the motor cortex just anterior to the precentral gyrus where the neurosurgeon found a neoplasm

The physiology above described applies to the primates as well as to the human subject In the human being still another set of coordinating engrams has been developed still farther forward for the function of language In the convolution of Broca are engrams for coordination of the muscles of the larynx, pharynx tongue and the mouth area in general to make the movements which are necessary for speech A lesion confined to that convolution leaves the muscles used in speech functioning as well as ever for all purposes except for speech itself Just anterior to Broca s convolution is the pars triangularis of the third frontal convolution essential to the motor functions of music including singing and instrumental music These patterns are laid down simultaneously on the two sides but as a rule better on the major side

Many students of aphasia have not yet succeeded in freeing themselves from the faulty concept that " a lesion of Broca s convolution causes Broca's aphasia and by Broca s aphasia frequently is understood the repetition of the same word or few words over and over again The facts are that a lesion of Broca's convolu

tion renders the patient unable to use his usual motor patterns for articulation of words After he has thus been deprived he does the best he can with the remainder of his patterns Some patients so afflicted cannot say a word others can say a few words usually the same ones over and over Still others can talk considerably the amount depends entirely on how successfully the individual has trained the minor area of Broca It will be shown subsequently that there are other possible causes for speechlessness the patient may for example have lost all power of language formulation from a lesion of the temporal lobe

At the foot of the left second frontal convolution is another set of engrams formed for the purpose of writing Exner s writing center This center is exactly analogous to Broca s convolution A lesion of it produces agraphia apractic agraphia

It must be clear without detailed elaboration that Broca s convolution cannot speak nor can Exner s center write without impulses reaching them from another portion of the brain where language is formulated for the expression of a concept An isolated speech or writing center is as helpless as though the engrams in it were out of function The mechanism of language formulation and of concept expression will be explained below

Anatomical Basis of Concepts

In the foregoing presentation the sensory perception was traced into the sphere of recognition and the outgoing motor mechanism was traced from the lowest level of association to the pyramidal tract This is another way of saying that the incoming projection system was followed through to the first step in association mechanisms and that the last step in association that of outgoing impulses was traced to the projection fiber system These physiologically lower areas are not concerned with the anatomical basis of concepts all of which is on a higher level The anatomical basis of concepts will now be presented ontogenetically

When an infant first sees a given object a memory of that visual impression is left in area 18 for future recognition Simultaneously another engram is formed in area 19 The one in area 18 is only for recognition it is of no use in concept formation The one in area 19 is for recall activation in an engram of area 19 revisualizes the object in question The engrams of area 19 are therefore subject to stimulation from other portions of the cerebral cortex not from area 17 in other words from above not from below in a physiological sense

Now if the object under discussion can only be seen the engram in area 19 representative of that object is the only engram formed But if it is simultaneously or subsequently also heard felt tasted or smelled other engrams are formed in the appropriate areas Area 19 is the tertiary visual area The tertiary auditory

area is in the temporal lobes downward and backward from the area of Wernicke The tertiary area for general sensation is in the superior parietal lobule For taste, according to Foerster and others, it is in the pararolandic opercular cortex For smell it is in the hippocampal gyrus

Thus, if the object in question is bacon frying in a pan, the visual impression of the bacon and its grease the sound of the grease as it spatters the smell and taste the feel of the crispness in the mouth, all will form the combined engrams of the concept of frying and fried bacon Later in life, as the source of the bacon becomes a matter of knowledge, the process of slaughtering will enter into the concept and perhaps even the raising of hogs and the whole art of animal husbandry and farming may enter into the total concept of bacon The tertiary sensory areas are then the seat of engrams, which form only a part of the concept of bacon engrams throughout the brain become the anatomical basis of the concept of bacon

The development of meanings to things is the development of the concepts, part of the concept engram system Recall of the concept will begin with reactivation of engrams in those tertiary areas

Up to this point language has been ignored in the discussion of engrams of concepts A little introspection will show that one may have extensive concepts without any language symbol to represent them Thus illiterates may learn mathematics without knowing how to express themselves Children have many concepts before they can understand language or speak This fact is of great importance in aphasia, because whenever a normal person speaks, he expresses concepts and the physiology of language requires one to begin with the idea and find the symbolic equivalent in language On the other hand, certain mental patients who are totally incapable of clear concepts, display logorrhea, a veritable flow of words without corresponding concepts We thus have concepts without language components and language without concepts The two sets of engrams, (1) of language and (2) of concepts without language components, are overlapped to some extent in the cortex but they are capable of independent function The manner of formation of language engrams and in which associations are formed between the two sets of engrams will now be presented

Anatomical Basis of a Word and of Language — Aphasia

When a child first *sees* bacon and its mother says, " that is bacon ", the child forms an engram in the area of Wernicke corresponding to the sound of the word The word will now be recognized when it is heard, but the child does not have any concept of the word unless he comprehends it i e unless the word acquires a significance If he learns that it is food that it has a certain taste and smell, that

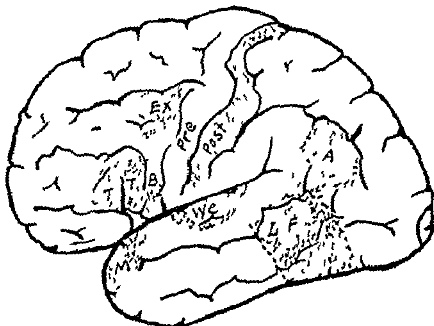


FIG 3 — Diagram of areas of greatest importance in aphasia Ex = Exner's writing center Pre and Post = the pre and post rolandic gyri T T = pars triangularis of the third frontal convolution B = Broca's convolution We = Wernicke's area A = angular gyrus L F = language formulation area

it has a pleasant or unpleasant connotation the word acquires significance and he forms a concept of it Thus engrams beyond those of recognition are necessary for concept formation In other words he must be able to recall the word before it has any significance for him at the moment Anatomically speaking engrams must be formed in the temporal lobe between area 18 the occipital area for visual recognition and Wernicke's area before auditory recall is possible when one has the concept in mind and needs the corresponding verbal designation Loss of this power of recall is *amnestic aphasia*

When the child has *heard* the word bacon a number of times he usually attempts to pronounce it When he does so he forms another engram this time in Broca's convolution and this engram immediately becomes associated with the one in the temporal lobe through the mediation of the external capsule From that time on whenever he hears the word bacon he almost automatically says it perhaps silently Furthermore whenever he sees bacon he tends to re hear and re say the word The anatomy of his engrams of the word bacon remains firm

ited to the auditory and motor engrams with their associations until he begins to read

When he *reads* the word, bacon, he forms another engram, this time in the angular gyrus The first engram formed there is one for recognition of the word It is of great importance in aphasia that at first, whenever he recognizes the written or printed word, he is told "that word is bacon" He thus invariably establishes an immediate association between the written word and the sound of the word and as he pronounces the word also, he simultaneously forms a motor engram in Broca s convolution intimately associated with the other two Many persons never become trained beyond this point and read only by recalling the sound and the motor equivalent For such persons these associations remain indispensable for reading and a lesion of Broca's area or of Wernicke s area will render the individual incapable of reading, even though the cortex of the angular gyrus remains intact Those who become effectually trained to silent reading will not lose the ability to read, unless a lesion actually effects the angular gyrus, or separates it from the visual cortex This point has been established thoroughly by the work of Henschen and has clarified the formerly incomprehensible alexias due to frontal or temporal lesions It also explains why destruction of Wernicke s area causes alexia a matter which Wernicke never explained

When the child begins to *write* he forms another set of engrams In Exner s writing center at the foot of the second frontal convolution of the major side anterior to the precentral gyrus he forms motor engrams for making the movements necessary for writing At first he only *copies* the words and does not have to revisualize them to do so However, he usually pronounces the words he writes and thus establishes associations with the motor engrams in Broca s convolution at the time Some persons retain this association as a necessity for writing about half of all persons free themselves from it later For this reason destruction of Broca s convolution in about half of all persons causes agraphia, in the other half not

When spontaneous writing begins the child must of necessity be able to *recall* the words to be written His engrams of words at the time already consist of a set of associated engrams in (1) the temporal lobe below Wernicke s area for recall of the auditory components, (2) Broca s convolution for memory of the movements necessary for pronunciation (3) the parietal lobe for kinesthetic memory of how the movements of the vocal organs *feel* in pronunciation proprioceptive sense and (4) the engrams in Exner s writing center and the corresponding engrams in the parietal lobe A new set of engrams which have been formed but not hitherto used must be activated in the angular gyrus for recall the revisualization of the appearance of the words to be written It is thus seen that five sets of associated engrams are in simultaneous use in spontaneous *writing of words*

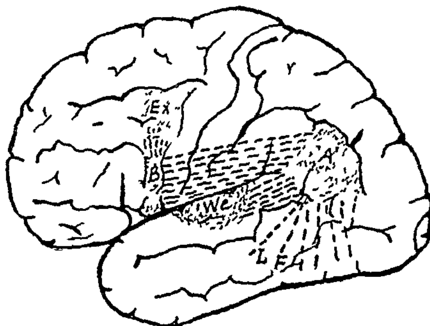


Fig 4 — The writin mechani m (imple t po ibl diagram) Ex = Exner frontal writ ing center B = convoluti n of Bro a A an ular gyrus W = area of Wernicke L.F = lan uage formulation area

However the *writing of words* is not writing of language Language involves inflection of nouns pronouns adjectives and adverbs and also conjugation of verbs with their tenses and moods Preferably there should be also evidence of rhetoric in language and the whole system hould be applied to a theme i e to the expression of concepts This function of language formulation depends on another set of engrams in the posterior portion of the temporal lobe chiefly area 37 of Brodmann A lesion of that area gives rise to amnesic aphasia difficulty with recall of words sometimes chiefly nouns If only nouns fail to be recalled the clinical syndrome is called *anomia* *Amnesic aphasia* might better be called *formulation aphasia*

Even with all of this writing mechanism intact there is a possibility of interference with writing by the occurrence of other forms of apraxia which have not been described up to this point One of these is *ideokinetic apraxia* another is *Kleist's constructive apraxia* The former will be described under the heading of apraxia the latter must be described here Kleist found that lesions of the border between the angular gyrus and area 19 caused the patient to lose the sense

ited to the auditory and motor engrams with their associations until he begins to read

When he *reads* the word, bacon, he forms another engram, this time in the angular gyrus The first engram formed there is one for recognition of the word It is of great importance in aphasia that at first, whenever he recognizes the written or printed word he is told, " that word is bacon He thus invariably establishes an immediate association between the written word and the sound of the word and as he pronounces the word also, he simultaneously forms a motor engram in Broca s convolution intimately associated with the other two Many persons never become trained beyond this point and read only by recalling the sound and the motor equivalent For such persons these associations remain indispensable for reading and a lesion of Broca's area or of Wernicke s area will render the individual incapable of reading even though the cortex of the angular gyrus remains intact Those who become effectually trained to silent reading will not lose the ability to read unless a lesion actually effects the angular gyrus or separates it from the visual cortex This point has been established thoroughly by the work of Henschen and has clarified the formerly incomprehensible alexias due to frontal or temporal lesions It also explains why destruction of Wernicke s area causes alexia a matter which Wernicke never explained

When the child begins to *write* he forms another set of engrams In Exner s writing center at the foot of the second frontal convolution of the major side anterior to the precentral gyrus he forms motor engrams for making the movements necessary for writing At first he only *copies* the words and does not have to revisualize them to do so However he usually pronounces the words he writes and thus establishes associations with the motor engrams in Broca s convolution at the time Some persons retain this association as a necessity for writing about half of all persons free themselves from it later For this reason destruction of Broca's convolution in about half of all persons causes agraphia, in the other half not

When spontaneous writing begins the child must of necessity be able to *recall* the words to be written His engrams of words at the time already consist of a set of associated engrams in (1) the temporal lobe below Wernicke s area for recall of the auditory components, (2) Broca's convolution for memory of the movements necessary for pronunciation, (3) the parietal lobe for kinesthetic memory of how the movements of the vocal organs *feel* in pronunciation, proprioceptive sense and (4) the engrams in Exner s writing center and the corresponding engrams in the parietal lobe A new set of engrams which have been formed but not hitherto used must be activated in the angular gyrus for recall the revisualization of the appearance of the words to be written It is thus seen that five sets of associated engrams are in simultaneous use in spontaneous *writing of words*

isthmus is the great cross roads between the two a lesion there produces usually complete aphasia This theme is elaborated subsequently

Ideo kinetic Apraxia Ideational Apraxia and the Concept of an Act

Of the apraxias only cortical motor pattern apraxia and constructive apraxia have been discussed For the understanding of ideo kinetic apraxia and ideational apraxia it is necessary to present the physiology of an act

The motivation of every act is an emotional desire but that fact and the necessary anatomy does not need to be discussed further because the patterns for the execution of an act are all cortical and the connection are through the association tracts *The act once started will go on to the satisfaction of the* emotions if possible

If for purposes of discussion we consider so simple an act as putting one s finger to one s nose at the request of another the following cortical mechanism is set into motion The request is heard and interpreted through the engrams of language as already outlined Next an ideational motor plan is formed This means that the body scheme is visualized impulses travel to the occipital parietal and frontal lobes and the set of engrams to be utilized is placed in readiness A disturbance of this planning mechanism is called ideational apraxia and it results from a diffuse lesion such as multiple vascular or neoplastic lesions or from a toxemia Of the toxemias bromide poisoning is classical The patient behaves as though he were extremely absent minded though every element of the act is executed correctly

A patient of mine with bromide poisoning attempted to strike a match on the sole of his bare foot and could not understand why he failed He asked for one match after another until reminded that he needed the box When the box was provided he struck the match but held it in his hand while he talked until the match burned his finger

Another patient with multiple melanomata while dressing pulled his trousers up repeatedly but always forgot to put his suspenders on his shoulders As the trousers sank to the floor time and again he gave up and attempted to put on his shoes and socks He put both socks on one foot and then had difficulty in getting the corresponding shoe on

If the ideational plan succeeds it seems from clinico pathological cases to be correlated in the region of the supramarginal gyrus For purposes of diagnosis in focal lesions that general area may be considered the focus for motor plans but one must keep clearly in mind that there is no specific cortical zone for the purpose

of ocular guidance of hand movements In such cases the patient can write better with eyes closed than he can with them open Dentists, when learning to work by mirror guidance at first have great trouble in learning to reverse direction as seen in the mirror Anyone can demonstrate the difficulty to himself by attempting to follow irregular lines on paper by the use of a mirror A lesion causing constructive apraxia causes '*isolated agraphia*', i e, agraphia which is the only aphasic symptom in a case A lesion of Exner s writing center also may cause 'isolated agraphia'

Because of the great complexity of the engram system used in spontaneous writing it is relatively easy for any cerebral lesion of the major side to produce agraphia, and one should never make a diagnosis of a localized lesion on the basis of agraphia alone All other symptoms must be taken into account, especially those due to lesions of the projection fiber systems

Of course, the language formulation area, described above, functions not only in spontaneous writing but in spontaneous speech The difficulties of training it to perfection are obvious from the poor grammar and rhetoric heard in extemporaneous speeches Indeed relatively few learn to express themselves accurately and succinctly even in writing Much of such difficulty, however, is due to lack of clarity of concepts to be expressed in language The speaker who arises with muddled thoughts certainly will also have muddled language formulation Yet when the concepts are clear it is not always easy to find the exact words to express them This is evident in the difficulty persons have in recalling the names of acquaintances in casual meeting

A similar presentation might be given of the language of music, but as the fundamental principles are identical this is not necessary The sensory cortical area for music is as stated at the anterior extremity of the temporal lobe The motor area is the pars triangularis of the third frontal convolution One cannot discuss interpretation meaning or significance of music as one can of verbal language but the principle of recall is the same

From this presentation it is seen how complex the anatomical basis of even a word is in the cerebral cortex The complexity of language is even greater, because it takes into consideration also the engrams of language formulation

Now, this complex engram system of language is a unit in the sense that it is the system to be set into activity whenever a concept is to be expressed Whenever one speaks or writes one begins with the concept engram system and seeks the corresponding language system When one listens to a talk or when one reads a dissertation one begins with the language engram system and through it recalls the concepts

Aphasia in the broad sense consists in failure to make the connection between concept engram system and language engram system and because the temporal

isthmus is the great cross roads between the two a lesion there produces usually complete aphasia This theme is elaborated subsequently

IDEO KINETIC APRAXIA IDEATIONAL APRAXIA AND THE CONCEPT OF AN ACT

Of the apraxias only cortical motor pattern apraxia and constructive apraxia have been discussed For the understanding of ideo kinetic apraxia and ideational apraxia it is necessary to present the physiology of an act

The motivation of every act is an emotional desire but that fact and the necessary anatomy does not need to be discussed further because the patterns for the execution of an act are all cortical and the connections are through the association tracts *The act once started will go on to the satisfaction of the emotions if possible*

If for purposes of discussion we consider so simple an act as putting one s finger to one s nose at the request of another the following cortical mechanism is *set into motion The request is heard and interpreted through the engrams of* language as already outlined Next an ideational motor plan is formed This means that the body scheme is visualized impulses travel to the occipital parietal and frontal lobes and the set of engrams to be utiliz d is placed in readiness A *disturbance of this planning mechanism is called ideational apraxia and it results* from a diffuse lesion such as multiple vascular or neoplastic lesions or from a toxemia Of the toxemias bromide poisoning is classical The patient behaves as though he were extremely absent minded though every element of the act is executed correctly

A patient of mine with bromide poisoning attempted to strike a match on the sole of his bare foot and could not understand why he failed He asked for one match after another until reminded that he needed the box When the box was provided he struck the match but held it in his hand while he talked until the match burned his finger

Another patient with multiple melanomata while dressing pulled his trousers up repeatedly but always forgot to put his suspenders on his shoulders As the trousers sank to the floor time and again he gave up and attempted to put on his shoes and socks He put both socks on one foot and then had difficulty in getting the corresponding shoe on

If the ideational plan succeeds it seems from clinico pathological cases to be correlated in the region of the supramarginal gyrus For purposes of diagnosis in focal lesions that general area may be considered the focus for motor plans but one must keep clearly in mind that there is no specific cortical zone for the purpose

Now the ideational plan must be conveyed to the precentral gyrus so that the patterns for the movement may be properly coordinated In most persons an ideational plan is easily formulated on either side of the brain but in those who use the major side alone, the corpus callosum is an important fiber tract for inter communication between the two sides In such persons lesions of the corpus callosum will have the result of preventing the ideational plan from reaching the minor precentral gyrus When the ideational plan is good but cannot be conveyed to the precentral gyrus, the clinical picture is that of ideo kinetic apraxia

The clinical picture of ideo kinetic apraxia is that of inability to execute requested or thought out movements while still able to make the same movements reflexly Thus, the patient may be totally unable to lick his lips on request, but if his lips become dry, he licks them without difficulty Or, he walks about reflexly but if asked to put one foot forward, he cannot figure out how to make *the movement Or in trying to put on his hat he merely raises his hand in the* air or clenches his fist Liepmann s patient in attempting to pour water into a glass held the glass in his left hand and poured the water on his head Of course, ideo kinetic apraxia causes agraphia the patient may not even know how to grasp a pencil

Ideo kinetic apraxia may be unilateral it may affect only the head only the upper limbs only the trunk or it may affect only the lower limbs In the corpus callosum lesions of the anterior portion cause apraxia, when they cause it at all in the upper part of the body, of the posterior portion the lower part of the body, etc But the splenium is concerned with visual fibers and lesions in it do not cause apraxia

Section of the corpus callosum do not cause apraxia but progressive lesions of it usually do This is due to the fact that the patient does not attempt to use the commissural tracts if they are sectioned he simply forms an ideational plan on each side of the brain But in case of neoplasm he attempts to use the diseased structure and hence has apraxia The patient recovers from apraxia, when his lesion becomes stationary

The Body Scheme

The body scheme or body pattern is the concept which a person has of the body the relations of its parts visually by general sensation or by recall Disturbance of the body scheme may occur on the level of recognition by vision touch or proprioceptive sensation or on the level of recall by revisualization or by *recall of general sensation*

The earliest description of such disturbances by Anton [4] consisted of imperception of actual change of important physiology rather than anatomy Anton

described unawareness of blindness and deafness The patient who is blind but unaware of the fact claims that he can see and attempts to describe objects held before him He usually uses indefinite or evasive terms The object is light not exactly white or gray but not dark It is an object not too long or too heavy but not as light as a feather The patient unaware of deafness pretends to hear and is usually talkative replying with irrelevant conversation Anton also described unawareness of auditory agnosia which is a frequent occurrence in Wernicke s aphasia

In 1914 Babinski [5] called attention to lack of awareness of hemiplegia affecting the minor limbs His patients denied their paralysis though acknowledging possession of the limbs He coined the term *anosognosia* for this syndrome a term which means agnosia for disease Had he known of Anton s work he would not have selected a general term for a specific defect the term means loss of recognition of disease in general The lesion causing anosognosia is located close to or in the thalamus usually isolating it from the entire pallium except the occipital lobe There an occasional exception regarding laterality is that in about 10 per cent of the cases the major limbs are affected otherwise the sign appears in left hemiplegia in right handed persons and vice versa

When a lesion of the minor thalamosupramarginal bundle occurs the patient nearly always will have a disturbance of the body scheme usually he will deny his own left upper limb when it is shown to him In a discussion with the patient usually he will admit that all persons have left sides and left upper limbs but he will insist that his own hand held up before his face belongs to the demonstrator After a few days to a few weeks he recover from the delusion as a rule

The disturbance may be of any degree He may say It doesn t look like my hand but when I see it is connected to the arm and the arm to my shoulder it must be mine In other instances he says It looks like mine but I can feel it is not and I must believe my feelings (cited from a case reported by Dr C W Olsen) In still other cases the patient will continue to deny the limb and cannot be argued out of hi conviction In one of my cases such a delusion lasted five years However regardless of whether the di turbance is an illusion or a delusion and whether he can be argued out of it or not the lesion will be found to affect the thalamosupramarginal fibers That localization has never failed to correspond to the clinica' syndrome One must keep in mind that that lesion doe not cau e the hemiplegia which is present also The lesion must extend to the internal capsule or to the motor cortex The hemianopia which almost invariably accompanies the syndrome results from the simultaneous lesion of the optic radiation

As stated above the disturbance of the body scheme resulting from a lesion of the minor hemisphere affects the opposite limbs only There are however

at the first episode Therefore, we know that the temporal and angular gyrus functions were moved without the motor function following suit

A man was born left handed but was made to write with his right hand from the age of 8 onward At the age of 68 he suffered a right cerebral thrombosis with aphasia While his case never came to autopsy, it is nevertheless crucial because he had a left hemiplegia with his aphasia This proves that he was still right brained for language He recovered from this episode but some months later suffered a similar attack with right hemiplegia In the second attack he had a complete agraphia with the right hand (it was strong enough for holding a pencil) but he was able to write very well with the left hand He, therefore had a writing mechanism on each side of the brain, but he did not have a language storage, language formulation area on both sides if he had had it, he would not have become aphasic with his left hemiplegia

I shall not multiply cases to prove the points to be made The facts are as one would expect Comprehension of spoken language is acquired earliest in life and is most easily re trained on the minor side after the major is destroyed Spoken language comes next, reading third and writing last Speaking anatomically the temporal lobe is trained most easily, Broca's convolution second the angular gyrus third and with great difficulty, the widespread writing mechanism last and with greatest difficulty In the functions of music there is relatively little majority, the minor side takes up the function easily after destruction of the major In the sphere of non language function there is apparenty a lack of major side training This statement applies *as a rule* with exceptions to the parietal and occipital lobes The body scheme functions are closely related to language so far as majority is concerned

In the clinical study of the agnosias and aphasias it is of the utmost importance to realize that after the destruction of a major functional unit, *whatever function of the nature in question the patient is capable of is performed by the minor side* For that reason the clinician must learn to recognize minor sided function The following paragraphs are an epitome of what has been painfully learned from hundreds of cases

The area of Wernicke of the minor side fatigues with great rapidity The patient with Wernicke s aphasia can be expected to comprehend the first five to six simple questions asked This fact often has led an examiner who was satisfied with two questions, to conclude that the patient had no aphasia We may say to him put your finger to your nose put your hand on top of your head and hold up two fingers , and obtain a perfect response That fact proves nothing about aphasia If one continues or if one asks a complicated question, it is soon found that the patient understands nothing said to him

Broca s area of the minor side is capable of a few words usually the same ones

over and over If the patient under examination says the same few words without ability to select we can conclude that the minor area of Broca is functioning That fact, however does not prove that the corresponding major area is destroyed What has happened to the major area is a matter for study Perhaps it is out of communication with the language formulation area perhaps Broca s area is isolated and hence cannot function or it may be destroyed

The minor angular gyrus usually is capable of very little function if indeed it is capable of any Thus if the patient cannot read except an occasional letter the minor angular gyrus is trying to do the work That fact however does not prove that the major gyrus is destroyed It may only be separated from the major area of Wernicke which would render it badly handicapped If Wernicke s area is destroyed the result is the same What has happened to the angular gyrus is thus a matter for further study

The minor language formulation area always can function to some extent after destruction of the major but its language is badly organized wrong words are used *paraphasia* or the desired words merely fail to come For this reason *Wernicke s aphasia is characterized by loquacity and with humorously paraphasic* language

The old syndrome of transcortical motor aphasia in which the patient cannot speak spontaneously but can repeat anything asked of him is simply due to function of the minor hemisphere The syndrome of transcortical sensory aphasia in which the patient can repeat what is said and can read off anything handed to him without any comprehension whatever is also due to function of the minor side Language is merely dissociated from the concepts

The Temporal Isthmus

The temporal isthmus is a narrow band of white matter between the posterior extremity of the insula and the posterior horn or body of the lateral ventricle Through this corridor pass all the fibers which connect the temporal and occipital lobes with the thalamus for execution of auditory and visual functions Besides all association fibers from the language formulation area to and back from Broca s convolution as well as the association fibers from the angular gyrus to Wernicke s area and vice versa pass through the isthmus For these reasons a lesion of the major temporal isthmus paralyzes *the entire language mechanism This was the* one important fact, misinterpreted which led Pierre Marie to his conclusions

Any lesion of the isthmus will cause also homonymous hemianopia as the optic radiation passes through it If therefore a case appears with complete aphasia and hemianopia but without hemiplegia one should give serious consideration to a lesion of the isthmus The patient may thus be speechless without

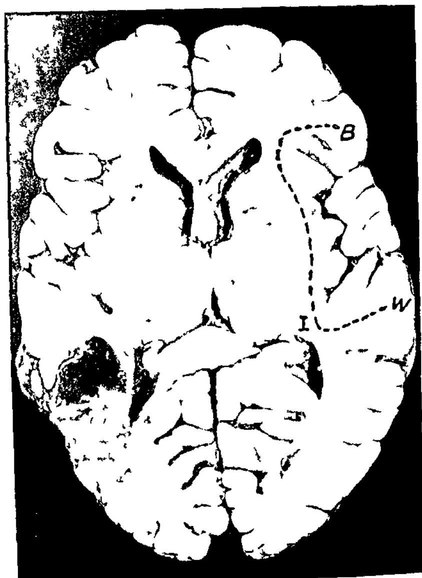


FIG 6 — Hemorrhage into left temporal lobe extending to temporal isthmus with complete aphasia Diagram on the right side shows path necessary in communication between Broca s and Wernicke s areas through the temporal isthmus I via the external capsule

having any involvement of Broca s convolution Lesions of the external capsule hemorrhages as a rule commonly extend into the temporal isthmus Any lesion of the external capsule alone separates Broca's convolution from the temporal lobe and hence causes aphasia

A lesion of the minor temporal isthmus gives rise to anosognosia or delusion

of the body scheme referable to the minor limbs Hemianopia is almost invariable in such cases

Examination of a Patient with Agnosia Apraxia or Aphasia

Before one starts an examination of a person suffering with a presumed aphasia one must ascertain that the patient is sufficiently clear in general mentation and sufficiently alert to cooperate Further one must make a careful general physical and neurological examination to be aware of a general toxemia such as uremia or bromidism and to determine such conditions as cortical blindness astereognosis or a severe cerebral arteriosclerosis or meningovascular syphilis which may produce multiple lesions An homonymous hemianopia especially if right sided should put one on the alert for various degrees of visual agnosia In cases of cerebral neoplasm the aphasia is hardly ever conclusive because of pressure symptoms Small areas are not destroyed discretely

It is quite possible to outline a complete systematic examination which will be certain to discover every item but it is rarely possible to make such an examination except in multiple sittings because the patient will fatigue Furthermore there is practically always an obvious defect with which it is wise in interests of economy of time and patient s effort to begin

The general impression given when one attempts to interview the patient gives an important lead Thus a euphoric voluble patient talking with marked paraphasia suggests immediately a lesion of the major temporal lobe He could not talk so volubly even incorrectly with the major convolution of Broca out of function If on the other hand the patient is depressed and gives the appearance of chagrin at his helplessness in expression we expect to find that the major area of Broca is out of function If the patient shows poor attention does not comprehend questions and does not answer one must have in mind either a complete destruction of the major language area or a lesion in the major temporal isthmus

Because of easy fatigue of the minor language areas it is important to reach a diagnosis of the type of aphasia without a long and tedious process The following points should not take long to determine

1 Can the patient speak? If he does not speak spontaneously can he repeat what is said to him?

If he says a few words and usually the same ones over and over or if he only swears he is talking by means of the minor area of Broca If he can repeat what is said transcortical motor aphasia he is nevertheless using the minor area of Broca If he talks volubly but with marked paraphasia he is using the major area of Broca but the minor language formulation area

2 Can the patient comprehend spoken language? To test this function the

patient is given commands such as, "raise two fingers or "put your hand on your head" If he understands nothing, or if he understands a few simple commands only to fail completely after that, he *is attempting to use the minor area* of Wernicke

3 Can the patient recognize written or printed words? To test this function he is given a set of cards each containing a single word There should be half a dozen or more different words and multiple copies of each He is asked to place all cards with identical words in the same pile If he does not understand the request, he is shown first how to sort them out, after which the cards are shuffled It is well to use similar words to avoid the danger of recognition by mere general appearances Thus, laborer, laborious, laziness lassitude, lavatory, lascivious, lapdog or a similar set may be selected For this test he does not need to know their significance, he merely needs to recognize them

If he cannot sort them out, the angular gyrus of the major side is destroyed or separated from one or more of its important associates, occipital lobe area of Wernicke, occasionally even the area of Broca If it is separated from the occipital lobe, homonymous hemianopia will be present If it is separated from the area of Wernicke because of a destruction of that area, such a fact is already discovered If the patient can sort half a dozen words only to be completely fatigued, one can assume that he is doing the work with the minor area

4 Can the patient read with comprehension? If he recognizes words but fails to comprehend, he does so with the minor angular gyrus

5 Can the patient do simple calculations (calculations which would have been simple for him before he became ill)? If he cannot and one is certain that he understands the problem, he has a lesion of the major occipito parietal area

6 Can the patient write or only copy? Agraphia accompanies so many forms of aphasia that only isolated agraphia signifies a focal lesion Even in isolated agraphia there are two possible sites frontal and parieto occipital

7 Can the patient name objects shown him and formulate language well? If he has amnesic aphasia or paraphasia, he is attempting to formulate language with the minor area 37

Prognosis in Aphasia

The prognosis in aphasia is, first of all, based on the prognosis of the causative lesion If the aphasia is due to a neoplasm, one may as well proceed to remove the lesion and let the aphasia wait Of course, most aphasia is due to vascular lesions secondary to arteriosclerosis or trauma In arteriosclerosis with hemorrhage thrombosis or embolism the prognosis depends on the age of the patient, his general condition, recoverability from the lesion and his will to work at recov

ery as well as his intellectual capacity It is amazing at times to see a man or woman of 70 years refuse to remain aphasic and work diligently to re learn language and in other cases to see young persons resign themselves to their fate The rule is that young persons recover and old ones do not but the personality factor is of great importance

Nielsen and Raney have reported a series of cases of remarkable recovery *after complete destruction or even surgical removal of the major temporal lobe* In one case a dentist of about 40 years knowing that he had had a malignant growth removed, worked so diligently that he spoke and wrote exceedingly well in the two remaining years of his life He understood practically all that was said Several of the author s students of aphasia have become professional teachers of aphasics and have obtained some excellent results Singer and Low reported a case with recovery and with autopsy 25 years later The major area of Broca was completely absent

Treatment of Aphasics

The treatment of an aphasic patient depends on the fact that engrams of language are laid down in both hemispheres simultaneously and in homologous areas The engrams to be trained therefore are in existence but they are crude and have gone without use during most of the patient s life for which reason in most old patients the retraining must be cautious and gradual

The principles to be followed are exactly the principles used in teaching a foreigner English when the teacher does not know the student s native tongue In comprehension of spoken language pantomime is used extensively Objects are named repeatedly and distinctly while the object in question is exhibited The teacher s speech must be slow clear and painstakingly distinct Loud talk is not understood by the aphasic patient any better than is soft speech

When one is dealing with motor aphasia one must show the patient how to place the lips and tongue for each sound Exaggerated movements are demonstrated It is a good plan to have the patient write the word he is trying to say in order to give him as many associations as possible

Reading and writing are taught as one would teach a child If the right hand is paralyzed the left hand is to be trained This would be difficult in a young person and certainly it is more difficult late in life

BIBLIOGRAPHY*

1 BOUILLAUD J Recherches cliniques propres a demontrer que la perte de la parole correspond a la lesion des lobules anterieurs du cerveau et a confirmer l opinion de M Gall sur le siege de l organe du langage articule Arch gen de Med Paris 18 5 VIII 25

DAX M Lesions de la moitie gouche de l encephale coincident avec l oubli des signes de la pensee Montpellier 1836

3 BROCA P Sur le siege de la faculte du langage avec deux observations d aphemie Bull de la Soc anat Aout 1861

4 TROUSSEAU A De l aphasie Clinique medicale 186 , 1st ed

5 PICK A Beitrage zur Pathologie und pathologischen Anatomie des Central nervensystems Karger Berlin 1898

—— Studien uber motorische Apraxie Deuticke Leipzig und Wien 1905

—— Ueber das Sprachverstandnis Barth Leipzig 1909

6 JACKSON J HUGHLINGS Case of large cerebral tumor without optic neuritis and with left hemiplegia and imperception Royal London Ophthalmic Hosp Reports 1876 VIII 434

—— Affections of speech from disease of the brain Brain 1878–1879 I 304 reprinted in Brain 1915 XXX

—— Selected Writings of Hughlings Jackson edited by Taylor Hodder and Stoughton London 193

7 WERNICKE C Der aphasische Symptomencomplex 1874 Breslau reprinted in Gesammelte Aufsatze Fischer Berlin 1893

—— Lehrbuch der Gehirnkrankheiten Fischer Berlin 1881

—— The symptom complex of aphasia Diseases of the Nervous System Appleton p 65 New York 1911

8 KUSSMAUL A Die Storungen der Sprache 3rd ed Vogel Leipzig 1881

—— Disturbances of speech in Ziemssen s Cyclopaedia of the Practice of Medicine 1877 XIV 581

9 FREUD S Zur Auffassung der Aphasien Deuticke Leipzig und Wien 1891

10 DEJERINE J Semiologie des affections du système nerveux Masson et Cie, Paris 1914

11 STARR M ALLEN The pathology of sensory aphasia with an analysis of fifty cases in which Broca s center was not diseased Brain 1889 XII

12 MILLS C K The Nervous System and Its Diseases Lippincott Phila 1898

13 MARIE PIERRE International neurological congress Paris 1906

—— Travaux et memoires Tome premier Masson et Cie Paris 19 6

14 MOUTIER F L aphasie de Broca Steinheil Paris 1908

* There are not less than 3 500 articles on aphasia Bonvicini in Neurologie des Ohres by Alexander and Marburg wrote on aphasia only as it pertained to the temporal lobe but he gave 30 pages of references Those here given cover the subject Henschen s monograph [19] is a large quarto work in three volumes

15 LIEPMANN H Das Krankheitsbild der Apraxie (motorische Asymbolie) Monatschr f Psychiat u Neurol VIII 3 1900
—— Das weitere Krankheitsverlauf bei dem einseitig Apraktischen Monatschr f Psychiat u Neurol XVII–XIX 1 1906
—— Drei Aufsatze aus dem Apraxiegebiet Karger Berlin 1908
16 HEAD H Speech and cerebral localization Brain 1923 XLVI 355
17 CHARCOT J M Œuvres completes de J M Charcot Tome III Delahaje et Lecrosnier Paris 1887
CHARCOT J M and PITRES A Etude critique et clinique de la Doctrine des Localisations motrices Alcan Paris 1883
18 WILSON S A K Aphasia Kegan Paul Trench and Trubner London 1926
19 HENSCHEN S E Klinische und pathologische Beitrage zur Pathologie des Gehirns Nordiska Bokhandeln V VI and VII Stockholm und Leipzig 19 0–19
0 POTZL O Die Aphasielehre vom Standpunkte der klinischen Psychiatrie Bd I Deuticke Leipzig und Wien 1928
21 KLEIST K Gehirnpathologie Barth Leip ig 1934
22 NIELSEN J M Agnosia apraxia and aphasia Los Angeles Neurol Soc 1936
—— Textbook of Clinical Neurology Hoeber New York 1941
3 COBB S Speech disorders and their treatment Doherty and Runes 1943 Rehabilitation of the war injured Philo ophi al Library New York
24 ANTON G Ueber Herderkrankungen des Gehirns welche von Patienten selbst nicht wahrgenommen wurden Wien klin Wochenschr 1898
—— Ueber die Selbstwahrnehmungen der Herderkrankungen usw Arch f Psychiat 1899 XXXII 86
5 BABINSKI J Troubles particuliers de la conscience chez hemiplegies Rev neurol 1914 XX 845

October 1 1944

CHAPTER XI

DISEASES OF THE BASAL GANGLIA AND SUBTHALAMIC NUCLEI

By D DENNY BROWN

Table of Contents

CHAPTER XI

DISEASES OF THE BASAL GANGLIA AND SUBTHALAMIC NUCLEI

By D. DENNY BROWN

TABLE OF CONTENTS

ANATOMICAL CONSIDERATIONS

The general configuration of the basal ganglia has been described in the introductory chapter to this volume It will be recalled that the term includes the optic thalamus and the corpus striatum The latter in turn comprises two distinct divisions the caudate nucleus and the lenticular nucleus The lenticular nucleus is further divided into putamen and globus pallidus The comparative anatomists finding almost complete structural identity and neuronal connections between the caudate nucleus and putamen group these two nuclear masses in one unit the *striatum* (or neostriatum) as contrasted with the globus pallidus *pallidum* (or paleo striatum) The function of the optic thalamus is universally agreed to be related to sensory or afferent pathways In this section we are concerned with certain diseases of which the chief signs are disturbances of posture and movement and traceable to pathological changes in the corpus stri

atum or its descending pathways The more important of these structures are *represented diagrammatically in Fig 1*

The anatomical details of these pathways are extremely intricate, but in general it will be observed that there is a cascade of descending motor tracts beginning in the cerebral cortex and converging on the lower motor neuron chiefly of the opposite side Short circuiting these relays from the lower end of the mechanism are successively longer pathways, the olivospinal reticulospinal rubrospinal and corticospinal tracts Similar short circuits as viewed from the upper aspect are the corticostriate, corticopallidal, corticonigral, corticopontine and corticospinal connections Bridging across the mechanism are the cerebellar pathways with olivo and ponto cerebellar influx, and cerebello rubral and cere bello thalamo pallidal outflows It may be observed that the rubrospinal tract in man is very small, and that the formatio reticularis occupies an important position in the system

The regions of cerebral cortex connected to the striatum are thought to be the "suppressor bands" or inhibitory areas of the frontal and parietal regions[1] but particularly from the premotor cortex[3,4,5] Even in the motor cortex (area 4) some cells project into extrapyramidal motor structures as judged by the results of stimulation[6], but the course of these is not known Mettler's experiments[4] indicate that many are relayed through the striatum Whereas the larger cells in the basal ganglia are generally held to be those that project the interconnecting tracts, the distinction in function between the large and small cells hypothesized by Hunt[7] has not been confirmed

The endings of precentral and postcentral projection fibres on the neurons of the caudate nucleus appear to be unmedullated except for some fibres that run in the subcallosal fasciculus to the body and tail of the caudate nucleus[3] From the frontal area 6 fibres run to the substantia nigra as well as to the pons (frontopontine tract) Another large contribution to the corticonigral fibres comes from the olfactory cortex through the subthalamic peduncular fasciculus

In general it may be observed that in this complex network three fairly dis tinct subsidiary systems may be observed One is the corticostriate system with chief outflow through the substantia nigra The second is a thalamo pallidal subthalamico rubral system of connections Lastly there is the direct cortico nigral connection involving the compact part of the substantia nigra All these networks connect with the tegmental and pontine reticular substance and inferior olives from which the main spinal connections arise Extensive cross connec tions relate the striatum and substantia nigra with the pallidum It will be seen that the conception of the pallidum as the main executive organ of the striatum as advocated by the Vogts, has been replaced by that of a pallidorubral connection largely independent of the strionigral complex as introduced by Papez[3] For

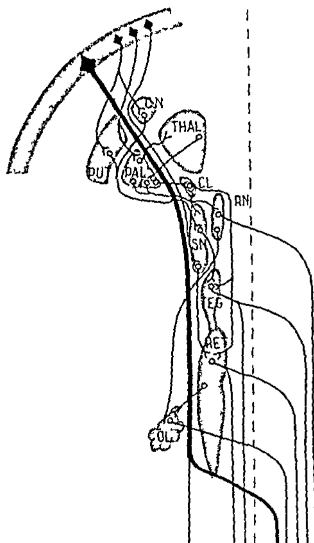


Fig 1 Diagram to show the chief connections of the basal ganglia with the motor system

the general anatomical and histological relationships of these nervous connections the reader is referred to the reviews by Papez[4] and Mettler[8]

The blood vessels supplying the corpus striatum have been studied by Aver and Aitken[9] and others reviewed recently by Alexander[10] and Rubinstein[11] The oral third of the caudate nucleus and putamen are supplied by the small directly perforating branches of the anterior cerebral artery including one larger branch the recurrent artery The remainder of both nuclei except the extreme tail of the caudate is supplied by a series of directly perforating branches of the middle cerebral artery The long anterior choroidal artery admirably discussed by Abbie[1], leaves the internal carotid just before it divides into middle and anterior cerebral branches and supplies the medial and intermediate segments of the globus pallidus and often, the whole of this nucleus as well as the posterior limb of the internal capsule, the subthalamic body of Luys and the extreme tail of the caudate nucleus The striopallidal veins drain into the vein of Galen as well as into tributaries of the cavernous sinus

Physiological Considerations

The diseases associated with pathological changes in the basal ganglia present one or other or combinations of a very characteristic group of disorders of movement In 1912 Wilson[13] used the adjective 'extra pyramidal' in relation to such disorder and contrasted it with the disturbance caused by lesions involving the corticospinal pyramidal system The clinical differences he sought to emphasize are as true and diagnostically valid today as they were then However the demonstration by Fulton and his colleagues[14 1] that spasticity ' in the sense exemplified by the posture and clasp knife rigidity of a capsular hemiplegia is an epiphenomenon which can, at any rate be dissociated in part from damage to the area of cortex giving origin to the Betz cells (area 4), left some doubt as to the correct description of ' pyramidal signs " The final blow to the clinical conception of disorder of the pyramidal system " was delivered by Sarah Tower[16] in her classic description of the monkey after section of the pyramid in the medulla It may be recalled that the activities of the animal after bilateral pyramidal section were limited to such postural patterns as are determined by the body righting reflexes (thalamic reflex pattern ' Magnus[18] Bieber and Fulton[19]) to progression (enfeebled and hindered by overadduction of the limbs and instability of the trunk), to certain patterned emotional responses of fear (flexion of upper limbs with clenched fists), desire (extension and circumduction of upper limbs followed by flexion and adduction) and threat (retraction of body with flexed upper limbs extended lower) All discrete use of the digits was lost but a weak grasp of the hand appeared in movements of progression

and was used in purposive movements The fingers were all hyperextended at the metacarpophalangeal joints but remained clawed at the interphalangeal joints The animal could not relax such a grasp voluntarily although anger or fright caused the hand to open widely There was no rigidity of muscles and correspondingly no clasp knife phenomenon The tendon jerks were ample but slow and pendular The abdominal reflexes were depressed Vasomotor responses in the limbs were defective but pilomotor reactions were present The associated movements of extension of the upper limb with yawning and flexion with strong biting were present After unilateral section associated movements in the affected upper limb mirrored flexion or extension pronation or supination in the sound limb An additional point of some importance is that the animal could graduate a purposive relaxation of the posture of the forelimbs as in stooping to grasp an object with the mouth In the chimpanzee[1] the disorder after pyramid section is even more profound We must not however fall into the error of supposing that the pyramidal tract is alone the mechanism of all the functions that are absent and indeed its only certain function is that of a pathway for certain discrete movements when initiated at cortical level The organization of the central nervous mechanism is based on a series of inter facilitating mechanisms and as Rioch has emphasized the removal of a large and powerful set may so disturb the levels of excitability at which the others work at any given locus as to block their activity The available evidence of extrapyramidal manifestations in the trunk and limbs then is of simple postural reactions with stereotyped movements of progression and emotional expression

In contrast the decorticate animal has an increased postural contraction in the extensors of the lower limbs and the flexors of the upper and has the same postural righting reactions The reflexes are brisk and all motor activity is stereotyped Much more extensive studies have been made on decorticate dogs than on monkeys and the descriptions of Mettler and associates and Bard and Rioch[1] reviewed by Rioch are recommended Such animals do not exhibit incessant activity but have an inability to initiate or inhibit movement suddenly Motor activity could be conditioned to relatively coarse auditory or visual stimuli The release of righting reflexes with corresponding postural pattern and the hyper activity of tendon reflexes and resistance to passive movement can be produced by excision of areas 4 (motor) and 6 (premotor) bilaterally without interference with the remaining cerebral cortex[9] In monkeys reflex grasping (proprioceptive arboreal righting reflex) is part of the thalamic posture so released and is found also in the grasp of the animal after section of the medullary pyramid Unilateral removal of areas 4 and 6 induces the spastic hemiparesis characteristic of human hemiplegia The spastic paresis thus produced is unaffected by section of the pyramid on the side of the paresis (Tower)

The postural pattern produced by decortication remains the same if the basal ganglia are included in the extirpation When the level of section reaches the midbrain, the resulting posture is profoundly modified, all four limbs being stiffly extended with very brisk tendon reflexes (" decerebrate rigidity ") The rigidity is much greater at the proximal joints The comparison of the flexed spastic posture of the upper limb of areas 4 and 6 extirpation and the extended posture of decerebrate rigidity is of interest in demonstrating the presence of some contrary mechanisms at cortical and brain stem levels the functional significance of which is unknown Area 6 of Brodmann, the frontal cortex immediately oral to the motor cortex proper (area 4), has small neurones which project on the striatum[1, 4] and on the substantia nigra and pontine nuclei [5] The most oral part of area 4 (area 4s) also projects on these structures, and stimulation of area 6 or 4s induces inhibition of posture on the entire opposite side of the body, even after section of the pyramid (Tower[10]) Similar inhibition was obtained by stimulation of the caudate nucleus or putamen by Mettler and Mettler [6], and these investigators claim to abolish the inhibition from area 6 by cocainization of the same nuclei Experimental damage to area 6 alone, if extensive appears to produce a very slight plastic rigidity without change in reflexes (personal observations) A spasticity of the opposite limbs is induced by excision of area 4s, which involves both pyramidal and parapyramidal projection It has, therefore, not been possible to reproduce true parkinsonism by damage to known extrapyramidal structures

Comparison between the decorticate animal with and without the caudate nuclei[1] indicates the release of leaping and the progressive movements in the latter without loss of defense and emotional reactions The animal still follows a moving object Kennard and Fulton [7] report a rhythmical tremor at a rate of 8 to 14 a second in some animals after bilateral frontal and caudate nuclear injury, but this only appeared when paresis was present The tremor accompanied all movement and posture Small isolated lesions of the caudate nucleus were without any effect (Wilson [8], Mettler[1] and others)

Whereas extensive bilateral damage has been produced experimentally in the pallidum by some investigators without symptoms [9], and stimulation of this nucleus in the intact brain is without effect, there seems to be clear indication that the hyperkinetic progressive movements seen after bilateral frontal and caudate extirpations are most highly integrated in the region of this nucleus The movements cease when the level of section reaches the midbrain After degeneration of the corticospinal fibers direct stimulation of the globus pallidus causes a tonic contraction of the ipsilateral limb (Mettler) with a tremor which varies in rate with the strength of stimulus In the intact animal stimulation of the pallidum during a movement of the opposite limb, induced by stimulation of the

cortex provokes a tonic posture in the limb maintained after cessation of the cortical stimulation (Rioch and Brenner) and plastic in quality (Mettler[5])

Stimulation of the subthalamic nucleus of Luys provokes a contraction of the dorsal midline musculature of the opposite side whereas stimulation of the red nucleus induces similar contraction of the axial musculature of the same side with ipsilateral flexion of the forelimb extension of the contralateral Stimulation of the substantia nigra results in increase in extensor posture chiefly on the opposite side of the body

Although it is difficult to infer function from the fragments of movements and postures produced by electrical stimulation we find no physiological evidence to support a view that the basal ganglia are concerned with any one category of motor activity Further it is to be emphasized that no convincing evidence of localization of muscles or limbs is seen in any one of the striate pallidal or subthalamic nuclei It is not an independent system for movement or posture No single functional pattern of motor response is identified with any one of these nuclei or indeed with any structure above the midbrain The essential mechanisms of locomotion are present in the spinal cord (Sherrington[31]) as are those of reciprocal innervation of micturition etc The righting reflexes appear to be mediated through the reticular substance in the pons (Lorent de No) and at least some pseudoaffective responses are obtainable after excluding structures above the midbrain

The physiological evidence does however indicate that the basal ganglia and subthalamic nuclei are essential for the motor integration of stereotyped behavior It is the means by which this is accomplished that eludes us Two chief divisions of function are indicated in the antagonism between striatal and pallidal function Moreover the controlling function exercised by the striatum is part of a wider system which includes the frontal and parietal cortex

The system of control of higher centers by lower has long been held to be primarily by suppression as enunciated by Jackson The doctrine of evolution implies the passage from the most organized to the least organized or in other terms from the most general to the most special Roughly we say that there is a gradual adding on of the more and more special, a continual adding on of new organizations But this adding on is at the same time a keeping down The higher nervous arrangements evolved out of the lower keep down those lower just as government evolved out of a nation controls as well as directs that nation The principle of release of lower centers by lesions of higher thus evolved by Jackson from the principle stated by Claude Bernard would appear to be abrogated by the recent observations of Tower on pyramid section This however is far from being the case for many observations indicate that the pyramidal tract ends on an internuncial neurone and not on the final motor neuron Of sup-

pression of intermediate centers by the cortex and of multiple kinds of suppression there is increasing evidence Did not centers 'resist' one another, there could be no independence of operations differentiation would be practically annulled On the other hand, if some centres could not overcome the resistance of others, discharge them by their own discharges, there would be no association of operations differentiation would be useless and, if there were not some order of 'resistances' and of 'dischangeabilities' there would be no orderly cooperation" ([33], p 453)

Some further insight into this system of controls is strongly suggested by studies of correlation of development of neuronal systems in the spinal cord and brain stem of anurian larvae In a series of fascinating studies Coghill[34 35 36] demonstrated conclusively that a tegmental center in such animals was responsible for coordinated activity, such as swimming, before local segmental reflexes and their nervous connections had matured The development of segmental reflexes in the limbs was achieved by fractionation of the earlier general pattern This process of isolation was accompanied by the development of an inhibition of the remainder of tegmental response Such a conception, now supported by studies of reflex development in the mammalian fetus is directly opposed to the earlier notions of elaboration of complex behavior by the compounding of simple spinal reflexes It gives an explanation of the curious dominance of the reticular formation (pontine and tegmental) over the spinal reflexes as seen in the phenomena of spinal shock and decerebrate rigidity Applied in a tentative way to the complicated basal ganglionic mechanism, which we have been considering, it would emphasize the interrelation of postural reactions (including all antigravity reflexes) with progression in the subthalamic region The further development of modification of this nervous level has the appearance not of a series of connections for this or that movement or function but as a differentiation by exclusion A cortical movement in such a conception would require a widespread inhibitory counterpart over all other postural or progressive reaction except that which aids and augments the movements desired Tower[18] has described the elaborate and unmistakeable posturing of the monkey with pyramidal section preparatory to grooming the skin only to find he was unable to make the movement The experimental and anatomical evidence is therefore very strongly suggestive that the system of higher control is exerted at various levels concurrently so that one or other aspect of the control of righting reflexes, simple antigravity posture or progression emotion etc can be integrated concurrently The removal of all types of control together by midbrain section leaves the confused caricature of total release of the reticulospinal mechanism called 'decerebrate rigidity'

If an oversimplification may be permitted, the following may suffice The

performance of skilled acts is not by a willed movement mechanism (pyramidal tract) in conflict with a postural mechanism (extrapyramidal tracts) Rather it resembles a setting of the main motor mechanism (bulbospinal) by means of a series of extrapyramidal adjustments (posture direction compensating movements) and a supply of power via the cortico pinal tract

Focal Lesions in the Basal Ganglia in Man

At this point the disorders of movement resulting from focal cerebral lesions may be considered particularly in their relation to the basal ganglia and sub thalamic connections

Although spastic hemiplegia is encountered most commonly as a result of damage involving the pyramidal tract the possibility of its occurrence without any damage to this tract was demonstrated by Bielschowsky[2] in 1918 in the de cription of the brains of two children affected by encephalitis Superficial necrosis of the cortex of one hemisphere had spared the Betz cells and the pyramidal tracts The paralyzed limb were severely pastic with contractured flexed fingers and wrists increased tendon jerks and ankle clonus The Babinski response was unhappily not recorded These ca es in the light of the physiological experiments of Fulton and Towers indicate that disturbance of the highest level of the motor mechanism namely the transcortical associations and extrapyramidal cortical projections can certainly lead to intense rigidity associated with most if not all of the phenomena of spasticity without involuntary movements

At the cortical level isolated lesions rarely elicit rigidity without damage to the motor area proper but the unusual condition described by Wilson and Walshe[38] as tonic innervation belongs to this class Their first case suffering from a right frontal tumor presented initially a hemiplegic rigidity with increased tendon jerks and an inability to relax a movement made with the left arm Unfortunately this type of disorder has not been studied in a patient with proven stationary lesion Damage entirely confined to the motor area proper (area 4) in man with complete description of the clinical state and anatomical findings has remained as elusive as a pure lesion of the medullary pyramid

The condition called flaccid hemiplegia usually has some increase in tendon jerks an extensor plantar re pon e and even some increased resistance to passive extension in the long flexors of the fingers In late stages the paralyzed fingers may become slightly clawed while movements at shoulder elbow and hip are partially retained without spastic resistance This condition may persist and has relation probably to pure lesion of area 4 or of the pyram d in the internal capsule although proof of such relationship is difficult to obtain

More commonly the flaccid hemiplegia becomes " spastic " This *spasticity* develops in the course of about three weeks and may be of various degrees according to the situation of the causative lesion A notable feature of late rigidity is a marked clawing of the fingers with flexion of the wrist and the elbow and the intensification of this posture by any attempt at voluntary movement with either the affected or sound limb In patients whose original lesion appears to have involved only motor and premotor cortex (e g cortical thrombophlebitis) and particularly, in young patients after a further variable interval, which may be weeks or months or sometimes years, the affected fingers begin to relax at the interphalangeal joints, and the phenomenon of spasticity with stiffly extended fingers is present At this stage the posture becomes unstable, and with effort or emotion the elbow extends, the wrist pronates and the hand closes and opens only after an interval This curious phenomenon heralds the appearance of *athetosis* which is only a further stage of instability of posture in which the affected fingers wander from over extended posture to over flexion Some control by willed effort is inevitable with such post hemiplegic athetosis, but the willed control is, at first only some ability to flex the fingers once they are extended later to extend them a little Extension always is weaker than flexion Willed effort affects all the fingers together, and the phenomenon of athetosis, or unstable hand, is inseparable from loss of individual movement The slow flexion or extension synergy can occur spontaneously in unpredictable sequences or can occur only on voluntary attempt at movement The movements on one side of the hand, either radial or ulnar, can be of the spontaneous variety, those on the other voluntary The " voluntary control requires at first considerable concentrated effort later the movement occurs with any effort such as making a movement with other limbs or an effort to speak The movements are then called " associated movements (Mitbewegungen)

These slow flexion and extension movements of the fingers associated with spastic hemiplegia were described in 1827 by Cazanvieilh[39] in his classical account of cortical hemiatrophy The condition had various names (" spasmoparalysis ', " spastic contracture ') until 1871, when Hammond[40] devised the word '*athetosis*' for similar movements occurring suddenly with sensory phenomena instead of a hemiplegia Hammond insisted at first that athetosis should continue in sleep which it seldom does Wier Mitchell[41] without reference to Hammond described a variety of these post hemiplegic movements which he called hemichorea " Gowers[4] in 1876 pointed the resemblance between athetosis and the post hemiplegic movements described above which he called " mobile spasm In time the objections raised by Hammond to the wider use of the word athetosis were overcome and all these conditions of unstable fluctuation between postures of flexion and extension in the fingers were called *athetosis* The toes often are

affected also but to a less degree. Occasionally to the slow changes in posture are added more jerky movements, especially if the patient became excited or made a sudden effort, and these are particularly evident in the proximal joints. The forearm might then suddenly extend or flex, the arm suddenly abduct, the face twitch, or the leg extend. Such movements, more in the tempo of Sydenham's chorea, cause the condition to be called *choreo athetosis*.

The situation of the lesions which lead to such involuntary movements has been cause for much discussion (see Schilder). Scars in the optic thalamus were found by Charcot[11] and a number of earlier writers, and the movements frequently are associated with the thalamic type of sensory disorder in the same limbs. The collected evidence reviewed by Martin and Alcock indicates that the essential structure is the corpus subthalamicum of Luys. Softening of this nucleus alone leads to wild, violent, incoordinate movements of the opposite limbs and face called "hemiballismus" by Economo but differing from chorea only in intensity. Damage to the neighboring internal capsule induces spasticity with slowing of the movements, which then resemble or are athetosis. If the oral pole of the nucleus is spared, the movements do not involve the face in some cases, although they were generalized in the example of Moersch and Kernohan. The "Bindearmchorea" of Kleist and others, attributed to lesion of the superior cerebellar peduncle in the brainstem, is in our opinion related rather to the neighboring nucleus of Luys and is a variety of hemiballismus. In exceptional cases, usually in the presence of an already existent hemiplegia, lesion of the red nucleus (Marie and Guillain) or dentate nucleus (Schilder) have induced athetosis.

In view of the relationship of Huntington's chorea and double athetosis to damage to the striatum without evidence of lesion of the corpus subthalamicum in most cases, it is of interest that focal lesions in the striatum also cause involuntary movements as in the classic example of Landouzy. Incessant athetoid movements of the hand and to a less degree of the foot began at the age of 2 and continued for 30 years. The only lesion found was a calcified mass in the lenticular nucleus of the opposite side. Davison and Goodhart[10] report choreiform movements of the left upper extremity alone with a lesion in the dorsolateral aspect of the right striatum. Not uncommonly a softening of the greater part of the putamen or whole striatum is found in patients without any involuntary movements having been noted during life.

Weil[3] insists that concomitant degeneration of the pallidonigrum is necessary before movements result from such lesions. The pathological evidence appears to be against this proposition, although more carefully studied cases are necessary to clear the objection completely. The claim of the Vogts[21] that localized damage to oral, middle or hinder third of the putamen results in movements of opposite face, arm and leg respectively is considerably weakened by the fact

More commonly the flaccid hemiplegia becomes "spastic" This *spasticity* develops in the course of about three weeks and may be of various degrees according to the situation of the causative lesion A notable feature of late rigidity is a marked clawing of the fingers with flexion of the wrist and the elbow and the intensification of this posture by any attempt at voluntary movement with either the affected or sound limb In patients whose original lesion appears to have involved only motor and premotor cortex (e g cortical thrombophlebitis) and particularly, in young patients after a further variable interval which may be weeks or months or sometimes years the affected fingers begin to relax at the interphalangeal joints and the phenomenon of spasticity with stiffly extended fingers is present At this stage the posture becomes unstable, and with effort or emotion the elbow extends, the wrist pronates and the hand closes and opens only after an interval This curious phenomenon heralds the appearance of *athetosis* which is only a further stage of instability of posture, in which the affected fingers wander from over extended posture to over flexion Some control by willed effort is inevitable with such post hemiplegic athetosis but the willed control is, at first, only some ability to flex the fingers once they are extended later to extend them a little Extension always is weaker than flexion Willed effort affects all the fingers together, and the phenomenon of athetosis, or unstable hand, is inseparable from loss of individual movement The slow flexion or extension synergy can occur spontaneously in unpredictable sequences or can occur only on voluntary attempt at movement The movements on one side of the hand either radial or ulnar, can be of the spontaneous variety those on the other voluntary The 'voluntary" control requires at first considerable concentrated effort later the movement occurs with any effort such as making a movement with other limbs or an effort to speak The movements are then called 'associated movements (Mitbewegungen)

These slow flexion and extension movements of the fingers associated with spastic hemiplegia were described in 1827 by Cazanvieilh[30] in his classical account of cortical hemiatrophy The condition had various names ("spasmoparalysis', 'spastic-contracture') until 1871 when Hammond[4] devised the word '*athetosis* for similar movements occurring suddenly with sensory phenomena instead of a hemiplegia Hammond insisted at first that athetosis should continue in sleep which it seldom does Wier Mitchell[41] without reference to Hammond described a variety of these post hemiplegic movements which he called "hemichorea" Gowers[4] in 1876 pointed the resemblance between athetosis and the post hemiplegic movements described above which he called ' mobile spasm In time the objections raised by Hammond to the wider use of the word athetosis were overcome and all these conditions of unstable fluctuation between postures of flexion and extension in the fingers were called *athetosis* The toes often are

affected also but to a less degree Occasionally to the slow changes in posture are added more jerky movements especially if the patient became excited or made a sudden effort and these are particularly evident in the proximal joints The forearm might then suddenly extend or flex the arm suddenly abduct the face twitch or the leg extend Such movements more in the tempo of Sydenham s chorea cause the condition to be called *choreo athetosis*

The situation of the lesions which lead to such involuntary movements has been cause for much discussion (see Schilder[3]) Scars in the optic thalamus were found by Charcot[44] and a number of earlier writers and the movements frequently are associated with the thalamic type of sensory disorder in the same limbs The collected evidence reviewed by Martin and Alcock[4] indicates that the essential structure is the corpus subthalamicum of Luys Softening of this nucleus alone leads to wild violent incoordinate movements of the opposite limbs and face called hemiballismus by Economo but differing from chorea only in intensity Damage to the neighboring internal capsule induces spasticity with slowing of the movements which then resemble or are athetosis If the oral pole of the nucleus is spared the movements do not involve the face in some cases although they were generalized in the example of Moersch and Kernohan[46] The ' Bindearmchorea of Kleist and others attributed to lesion of the superior cerebellar peduncle in the brainstem is in our opinion related rather to the neighboring nucleus of Luys and is a variety of hemiballismus In exceptional cases usually in the pre ence of an already existent hemiplegia lesion of the red nucleus (Marie and Guillain[47]) or dentate nucleus (Schilder) have induced athetosis

In view of the relationship of Huntington s chorea and double athetosis to damage to the striatum without evidence of lesion of the corpus subthalamicum in most cases it is of interest that focal lesions in the striatum al o cause involuntary movements as in the classic example of Landouzy[48] Incessant athetoid movements of the hand and to a less degree of the foot began at the age of and continued for 30 years The only lesion found was a calcified mass in the lenticular nucleus of the opposite side Davison and Goodhart[49] report choreiform movements of the left upper extremity alone with a lesion in the dorsolateral aspect of the right striatum *Not uncommonly a softening of the greater* part of the putamen or whole striatum is found in patients without any involuntary movements having been noted during life

Weil insists that concomitant degeneration of the pallidonigrum is necessary before movements result from such lesions The pathological evidence appears to be against this proposition although more carefully studied cases are necessary to clear the objection completely The claim of the Vogts[50] that localized damage to oral middle or hinder third of the putamen results in movements of opposite face, arm and leg respectively is considerably weakened by the fact

that the arm is involved almost always and the face or leg in only more severe states Often a more complete rigidity without movements has been caused by extension of a similar lesion into the capsule or cortex The degree of integrity of surrounding structures is, therefore, as important as the extent of damage to the nucleus concerned

More data obviously are needed before the mechanism of these involuntary movements can be elucidated Nevertheless we agree with the conclusions of Foerster that athetosis and chorea and dystonia are variants of the same process There is a great deal of evidence to indicate that at the midbrain level a variety of postural complexes are mediated in a manner which physiological experiment has not elucidated Certain distinct mechanisms do, however, appear to exert control One which we might call with Bucy and associates [3] *parapyramidal* extends from areas 6 and 4s in the cortex through the internal capsule to the pontine level Damage to this results in the phenomena of spasticity in paralyzed muscles with increased tendon reflexes Another is intimately concerned with the corpus subthalamicum Damage to this structure in the presence of some intact corticospinal innervation releases automatic activity in an unstable and incoordinate form If corticospinal innervation is destroyed also, subthalamic damage results only in an increase in the fixed rigidity with predominance of flexion of the fingers and toes but no movements If corticospinal innervation and subthalamic mechanism are both destroyed, additional damage to the superior cerebellar peduncle or red nucleus then can again release choreic instability It would appear that the striatum (caudate and lenticular nuclei) is in some way equivalent to the corpus subthalamicum, perhaps upstream in the same functional system so that damage at this level induces more complex incoordinations, the progressive play of postures of Huntington s chorea or double athetosis For the appearance of dystonic attitudes and movements the thalamic connection must be damaged In this sense the corpus subthalmicum may be thought to mediate a more coordinated series of postures than those which it in turn dominates in the tegmentum It is possible that the striatum coordinates those highly coordinate but aimless gropings and strivings which appear when it in turn is released from cortical control The antagonism between flexion and extension may well be a purposeless incoordination arising from the antagonism of separate controls of these processes by the pallidonigral region The major difficulty in physiological analysis is that presented by the fragments of movements presented in chorea dystonia and athetosis The Babinski extensor movement of the great toe is related in some way to the extensor element of athetosis and indeed both can be excited reflexly from any part of the body in some cases[54] as can the more common choreic movement in others The inconstancy of these phenomena does not permit any clear formulation of their mechanism at present

Set in the midst of the tangled net are the pallidum and substantia nigra Unsatisfactory though the experimental evidence may be the clinico pathological record again and again indicates these two as partners in a different mechanism from what has already been mentioned Its function is even less clear than that of the strio-subthalamic complex Its destruction brings about the generalized rigidity of parkinsonism combined with or independently of the other disorders mentioned above Focal damage to the region of the substantia nigra is reported in rare instances[54] to produce a contralateral extensor rigidity with pronation of the wrist and without reflex changes The postures of parkinsonism give no hint of the physiological process at fault unless it be that through the domination of whole musculature by the pallido nigral complex the cerebral cortex is given greater selectivity of control of the brain stem mechanism and that parkinsonism results from total release of this control

In a general sense all these disorders are motor incoordinations or interference with motor taxis A sensory disturbance closely resembling them is encountered sometimes This is the subcortical chorea of Wilson of which a good example was described also by Gowers[4] whose patient developed a wild incoordination on attempts at voluntary movement His right arm would fly over his head if he attempted to pick up a small object from the table Gowers found a parietal subcortical softening extending down to just reach the thalamus The movements of the fingers and hands which characterize athetosis and chorea were not present The often cited case of Miessl von Meyerndorf[39] was similar although complicated by an additional subthalamic lesion

Tremor is characteristic of two of the chief diseases of the corpus striatum and also is seen occasionally as rhythmic alternations of post hemiplegic chorea when this is violent The tremor then is present at rest but is not characteristic of paralysis agitans being usually a rhythmical pronation supination of the arm and sometimes concurrent tremor of the lips It occurs when the lesion encroaches upon the midbrain and especially the dentate nucleus[60] In terms of physiological mechanism tremor may be defined as the result of abnormally intense interaction of two opposing mechanisms In the complex interrelationship which the cortical striatal and pallidal control of tegmental centers undoubtedly possesses the interaction of an enhanced form of one with another at some common locus for example substantia nigra results in a reverberating circuit of inhibition excitation What the anatomical basis of this circuit may be is unknown It is certain that disturbance of the balance of innervation by further damage to cortico spinal innervation or by interference with the projection from area 6[53] can affect the tremor The different tremor of hepato lenticular degeneration is related to purposive contraction and appears to correlate with the lesions of the dentate nucleus and pontine nuclei consistently found in that disorder Provoca

that the arm is involved almost always and the face or leg in only more severe states Often a more complete rigidity without movements has been caused by extension of a similar lesion into the capsule or cortex The degree of integrity of surrounding structures is, therefore, as important as the extent of damage to the nucleus concerned

More data obviously are needed before the mechanism of these involuntary movements can be elucidated Nevertheless we agree with the conclusions of Foerster that athetosis and chorea and dystonia are variants of the same process There is a great deal of evidence to indicate that at the midbrain level a variety of postural complexes are mediated in a manner which physiological experiment has not elucidated Certain distinct mechanisms do, however, appear to exert control One which we might call with Bucy and associates [3] *parapyramidal,* extends from areas 6 and 4s in the cortex through the internal capsule to the pontine level Damage to this results in the phenomena of spasticity in paralyzed muscles with increased tendon reflexes Another is intimately concerned with the corpus subthalamicum Damage to this structure in the presence of some intact corticospinal innervation releases automatic activity in an unstable and incoordinate form If corticospinal innervation is destroyed also, subthalamic damage results only in an increase in the fixed rigidity with predominance of flexion of the fingers and toes but no movements If corticospinal innervation and subthalamic mechanism are both destroyed, additional damage to the superior cerebellar peduncle or red nucleus then can again release choreic instability It would appear that the striatum (caudate and lenticular nuclei) is in some way equivalent to the corpus subthalamicum, perhaps upstream in the same functional system so that damage at this level induces more complex incoordinations, the progressive play of postures of Huntington s chorea or double athetosis For the appearance of dystonic attitudes and movements the thalamic connection must be damaged In this sense the corpus subthalmicum may be thought to mediate a more coordinated series of postures than those which it in turn dominates in the tegmentum It is possible that the striatum coordinates those highly coordinate but aimless gropings and strivings which appear when it in turn is released from cortical control The antagonism between flexion and extension may well be a purposeless incoordination arising from the antagonism of separate controls of these processes by the pallidonigral region The major difficulty in physiological analysis is that presented by the fragments of movements presented in chorea dystonia and athetosis The Babinski extensor movement of the great toe is related in some way to the extensor element of athetosis and indeed both can be excited reflexly from any part of the body in some cases [4] as can the more common choreic movement in others[5] The inconstancy of these phenomena does not permit any clear formulation of their mechanism at present

poisoning or in the scarring process of double athetosis the damage may extend into neighboring white matter or involve one part of a ganglion in one case an other part in a second with or without patchy affection of variable parts of the cerebral cortex

It has been natural to seek explanations dependent upon peculiarities of the blood vessels which supply these structures An obvious example was the selec tive necrosis of the globus pallidus in carbon monoxide poisoning The abrupt angular turn of the small vessels which supply this ganglion presented a me chanical peculiarity which however is absent in the dog where the globus pallidus still preserves its special susceptibility

Hadfield [3] in a provocative paper on the subject of siderosis or deposits of iron in the brain gives evidence that it is only when siderosis is present that necrosis results from carbon monoxide poisoning Siderosis is progressive with age and in the di ease described by Hallervorden and Spatz the deposits become altogether excessive with resulting intense glial reaction Yet the mechanism of both physiological and pathological accumulation is unknown

The intense yellow taining of the basal ganglia together with the inferior olives in Kern icterus is a further example of a selective affinity of the basal ganglia Most inve tigators assume that a second factor for example anoxia besides jaundice is necessary for the staining or necrosis Simple obstructive jaundice has no particular effect on these organs Yet the effects of anoxia too are haphazard and have no special election as far as the ganglia are concerned It is possible that disorders such as siderosis are related to these grey masses because their solid structure may present differences from more superficial parts of the nervous system in the rates of renewal of tissue fluid

Two diseases with particular predilection for the basal ganglia namely paralysis agitans and Huntington s chorea share a type of cell change in which accumulation of lipoid within the cell is prominent Although this change is frequent and widespread it does not affect all the neurones at any one time thus differing from cerebro macular di ea e and from Niemann Pick s disease The chronicity of the process is such that probably only one stage in the evolution of the disorder in any one neurone presents the change Similar changes in cortical cells in pellagra and Korsakoff syndrome indicate however that some metabolic disorder is the probable cause

The onset of symptoms in all these diseases frequently is related to trauma Since no special effect of trauma alone has been demonstrated it has been as sumed that emotional factors which frequently alone precipitate the first signs are more important than the physical effect of trauma in drawing attention to or accelerating the disease processes

In both hepato lenticular degeneration and status marmoratus the primary

tion of tremor by such purposive contraction presumably indicates that cortico spinal innervation is one of the elements in rhythmic antagonism

General Pathological Considerations

In the accounts of the diseases with which this chapter is concerned certain considerations recur with sufficient regularity to deserve general comment First the disorders are all of that type called *degenerative* This of itself requires definition Modern medicine is not satisfied with the conception implied by "abiotrophy a premature ageing of isolated cell groups Indeed the clearest example of a striatal disease related to the germ plasm, Huntington's chorea exhibits a pathology which is much more reactive than that we know as simple atrophy Nevertheless so little do we know of the metabolism of nervous tissue that even in hepato lenticular degeneration where there is good reason to know the source of the noxa which underlies the disease, there is as yet no indication of its nature

Secondly, although the broad groups of these diseases each preserve a clinical form and a pathological picture which distinguish them from other morbid processes and which indicate that in each the brunt of the nervous damage falls on the basal ganglia, this localization is only relative Each affects other parts of the nervous system The first reaction to this revelation, a scepticism as to any correlation of 'extrapyramidal" symptomatology with damage to the basal ganglia is now generally relaxed in view of steadily accumulating evidence that damage to these structures is indeed accountable for a general class of disorder of motor function This acceptance was rendered more difficult by the fact that in these nervous organs the degree of motor disorder corresponds less with intensity of histological change than in any other part of the nervous system except possibly the hypothalamus This discrepancy is in part related to the masking of symptoms by concomitant pyramidal and parapyramidal deficit partly to lack of knowledge as to the means by which primary glial changes interfere with neuronal function The concept of diseases limited to the basal ganglia is vanishing and yet the clinical manifestations and symptomatic rationale remains essentially related to those ganglia or their connections

The peculiar susceptibilities of the basal ganglia have been discussed by many writers The hypothesis of 'pathoklisis" advanced by the Vogts[91] which presupposes peculiarities of physico chemical structure of the various nuclei which in turn lead to different susceptibilities to disease depends on the demonstrable differences in for example iron content which characterizes the globus pallidus and substantia nigra Yet the disease process seldom is localized to a single nucleus and in the necrotic forms such as Wilson s disease, carbon monoxide

PARALYSIS AGITANS

Synonyms — Parkinson's disease shaking palsy idiopathic or presenile parkinsonism

Definition

Paralysis agitans is a slowly progressive degenerative disease of the nervous system appearing in or after middle life and characterized by a combination of rigidity in the skeletal musculature with a tremor of distinctive type The rigidity greatly impedes muscular movements particularly movements of expression and tends to a fixity in posture Similar rigidities of whatever cause are included under the term parkinsonism sharing the plastic properties and absence of reflex changes which distinguish them from spasticity accompanying disturbances of direct cortico spinal innervation The tremor is characteristic in its regular rhythm and its lessening with movement and may also be included under the term parkinsonism Other types of parkinsonism will be discussed under *appropriate headings*

Etiology

The cause of paralysis agitans is unknown A history of the same disease in the family *is encountered in from 4 to 10 per cent of cases*[6 67 69 70] Inheritance is irregular Senile tremor in a distant relative is common and in the recorded families of cases[1] the occurrence of unusual features such as contracture of the fingers in flexion spasticity etc lead to doubt as to exclusion of unusual varieties of pseudosclerosis or other such disease These doubts are even stronger in relation to juvenile paralysis agitans (see progressive atrophy of the globus pallidus) Clear examples of paralysis agitans are however reported in siblings (Dellaert and associates[7] and others) Kehrer's[13] conclusion in favor *of a constitutional inborn liability is of interest in relation to the possible relationships to trauma and syphilis* As with many slowly progressive diseases *trauma often has closely preceded the onset in 16 per cent of cases* (*Patrick and Levy*) and the uncertainty *of this relationship is discussed further below Women are slightly less liable to be affected than men*[6] The disease is not limited to any country or racial stock and appears to be independent of level of nutrition

Historical

In a brief *monograph published in 1817 entitled* An Essay on the Shaking Palsy [7] James Parkinson a London physician gave a classical clinical description of this disease He mentions the differentiation between tremor at rest and

change occurs in the cerebral glia Although these changes are widespread in the brain, the first disorders of function usually are related to the basal ganglia Precipitation of the first symptoms by unrelated transient fever is particularly common in the second of these diseases This relationship, which has led to much confusion of etiology, still is unelucidated There appears to be no reason to associate the febrile disorders as such with the question of selectivity of basal ganglionic damage

The onset of some of these hereditary diseases soon after birth in relation to acquired infections and the demonstration of smallness of the basal ganglia in, for example, unaffected pre choreic members of Huntington s families have led Massalongo [4] and the Vogts to postulate an hereditary factor for an acquired disease a locus minoris resistentiae The essential process is, however, still that of the familial disease and we prefer to relate the effect to a general reaction of neurological abnormality already present

This chapter is concerned with diseases of which the chief manifestation is related to disorder of the basal ganglia Their classification is a matter of some difficulty for not only is their pathogenesis obscure but in some the exact structure primarily responsible for symptoms is uncertain These diseases and disorders are therefore, presented as clinical entities with such pathological evidence as entitles them to separate description They fall into four main groups

I Disorders in which parkinsonian rigidity, with or without static tremor, is the chief clinical sign
  (1) Paralysis Agitans
  (2) Post encephalitic Parkinsonism
  (3) Arteriosclerotic Parkinsonism
  (4) Parkinsonism following Intoxications

II Disorders in which variable rigidity and attitudes usually are associated with action tremor
  (1) Hepato lenticular Degeneration

III Disorders chiefly evidenced by variable rigidity with alternating swings of posture, which in more rapid sequence are athetoid
  (1) Dystonia Musculorum Deformans
  (2) Double Athetosis
  (3) Progressive Rigidity with Athetosis

IV Disorders resulting in a continual flow of athetoid movement with or without rigidity
  (1) Huntington s Chorea

It should be remarked that both post encephalitic parkinsonism and hepatolenticular degeneration may present combinations of items from all four main subdivisions of symptomatology

tal reactions will be discussed in a subsequent section There is no disorder of the sphincters or of the processes of digestion Increasing limitation of movement eventually leads to an existence entirely dependent upon nursing care after a period of 2 to 10 years from the first symptom Further progress of the disease then is associated with muscular contractures and the course is terminated by some intercurrent infection

Physical Signs

The rhythmical tremor of the resting limb the fixity of facial expression and the slowness of movement are so characteristic as to make them capable of recognition at a glance The early signs may however require some search and since moreover they may need differentiation from other forms of parkinsonism or the early signs of other forms of nervous disease they require separate description

Tremor — The tremor is first and most clearly developed in the small muscles of the hands the lips the tongue and the mandible Its rhythm is regular and slow about 3 to 5 beats a second The amplitude also is regular provided the state of muscular tension is not changed Contraction of the affected muscles damps the tremor and in its lesser degrees abolishes it often for a period of 1 to 10 seconds following the resumption of the original resting posture In its early stages complete relaxation of the affected muscles may abolish also the tremor but when fully developed it will appear in the affected parts whenever they are relaxed even in sleep [1] and may not be damped even on full muscular contraction In distinction from other forms of parkinsonism the tremor is a *gentle undulation* a rhythmic agitation and *is limited* to the periphery of the limbs the tongue lips and masseters There is no tremor of the head although movement may be transmitted from the lower limbs and the rhythmical jerking seen in so many post encephalitic parkinsonisms *is foreign to the idiopathic disease*

The beats of the tremor are concurrent in all parts although sometimes each beat may be delayed in the lower limb as compared with the hand so that as Brissaud[2] remarks the origin of the tremor must have some single central mechanism

In the hands the tremor consists of an alternate flexion extension of the fingers in unison at the metacarpo phalangeal joints the thumb beating against the index finger in adduction opposition From the rubbing of the first finger against the thumb the movement is called pill rolling as in the making of pills by hand A slight alternating flexion extension of wrist less commonly of elbow accompanies the corresponding phases of the finger movement Pronation supination is uncommon in idiopathic paralysis agitans A corresponding flexion extension of ankles appears later in the course of the disease causing a tapping of the resting foot as the patient sits but disappearing on standing Tremor

tremor on movement by Sylvius (1614–72) and the passing mention of festinating gait by Gaub (1758) and others in terms which appear to indicate its presence even in ancient times Parkinson differentiated the disorder from transitory choreas and morbus sacer', which appears to have included all varieties of chorea and athetosis, and from the tremors of alcoholism and advanced age He proposed the name paralysis agitans The disorder, so well described by Parkinson at first was confused with multiple sclerosis until the recognition of that disease by Cohen , Charcot and Ordenstein [6] It was classed among the neuroses until the beginning of the present century but only in the sense that there was no known pathology Agreement upon pathological changes first described in 1904 by Manchot and later amplified by Jelgersma[16] and Lewy [9] was not generally reached until after the dramatic demonstration in 1912 by Wilson that the similar condition of progressive lenticular degeneration depended upon gross lesions of similar parts of the nervous system The many contributions to the pathology of the disease from that time onwards will be discussed further in subsequent paragraphs

Symptomatology

The disease first manifests itself in the limbs of one side, before long however becoming bilateral and approximately symmetrical In rare cases the onset is in all four limbs concurrently The attention of the patient may first be drawn to tremor in the hand or to slowness in movement in the lower limb, and in some the slowness and fixity of expression may be noticed by others before the patient is aware of disability The most usual mode of onset is in the appearance of a gently alternating tremor of the wrist or fingers when at rest, gradually worsening in the course of weeks or months and then being accompanied by some slowness in movements such as writing lack of associated movements such as swinging the arms in walking and fixity of facial expression The lower limb then begins to show occasionally the rhythmical tremor at ankle and knee and appears to lag in walking In some patients the toes of the affected foot curl under in a rigid uncomfortable position at this stage Affection of both sides is accompanied by difficulty in initiating movement by progressive slowing of gait and shortening of steps and in late stages in difficulty in maintaining balance All movements become slow, speech is poorly articulated, tremor is incessant in all states except extreme exertion or in sleep and involves the lips and tongue Movements of the eyes usually are not affected Mastication becomes slow and inefficient late in the disease but respiration swallowing and digestion are unimpaired

There is no accompanying disorder of the mind or of the senses so that subject to the limitations imposed upon expression, the patient maintains a lively interest in his surroundings and an acute awareness of his disability Later men

does not cause the distortions of the neck or trunk seen in post encephalitic parkinsonism For many years a mildly flexed attitude capable of being over come by a powerful effort is the postural pattern

The effects of this rigidity are seen in the embarrassment of all varieties of *movement particularly chewing swallowing and speech as well as those men* tioned earlier The lack of reflex swallowing allows the accumulation of saliva in the mouth with resulting drooling from the lips The speech becomes monoto nous with incompletely articulated syllables so that one word runs into another The handwriting becomes smaller as well as tremulous and great difficulty is found in small movements such as buttoning clothes Since the proximal muscles are affected early there is great difficulty in getting an arm into the sleeve of a coat or of approximating the feet when they are separated The limbs first affected by tremor also are affected first by rigidity but if the tremor has ap peared first the development of rigidity dampens the tremor to some extent so that another limb later becoming tremulous may give the appearance of different distribution of tremor and rigidity The second limb in time will become rigid also

A remarkable effect is seen in the difficulty with which a patient with both slowing of movement and rigid fixity of posture maintains his balance If he leans a little too far backward he makes a series of small steps and too late so that he may have to continue stepping backwards retropulsion until he at last rights his balance or falls On leaning forward a similar series of short steps is necessary to regain his control of gravity All his forward progression may be in hurried short steps for the same reason the phenomenon of ' festination , which was noticed by writers before the time of Parkinson

We have spoken above of the usually accepted view that the delay in initia tion and slowness in execution of movement bradykinesia are due to the difficulty in overcoming rigidity A very striking feature is seen however in all but very advanced cases With a sudden strong emotional stimulus the patient can for a moment perform a rapid well coordinated movement such as rising rapidly from a chair jumping from a step or kicking a football to quote three examples in the writer s experience with a speed of which he had been hitherto and forever after entirely incapable Likewise in an earlier stage of the disease a patient whose gait is one of short shuffling steps can at times after much deliberation and false starts make a series of great strides which then he can continue for 50 to 100 yards coming to a sudden relapse of his ordinary status when fatigue or tremor induce the first falter The process requires some previous deliberation and effort which occasions great subsequent fatigue In some patients a sudden melting of the rigidity in both flexors and extensors together can be felt just before a movement begins in either one of these[34] These features indicate that the con

of the toes is unusual Tremor of the lips and tongue is seen at first only in some transitory posture and is constant only late in the disease when it involves the vocal cords and palate also In the eyelids the tremor is seen as a rhythmical blepharoclonus with the lids lightly closed, but this is less common in idiopathic paralysis agitans than other varieties Electromyographic studies by Cobb[1] and others reviewed by Rioch[4], Hoefer[8] and others indicate that each beat of tremor is a series of action currents, sharply demarcated from an interval of relative absence of discharge The regularity of pattern is completely characteristic of parkinsonian tremor as compared with other types[93] The beats alternate in opposing muscles There is no corresponding rhythm in the electroencephalogram

Rigidity —Most of the phenomena characteristic of the disorder are related to a stiffness of muscles It is doubtful if there is any true paralysis or loss of power of contraction, even in late stages Certainly the earliest affection of movement, the infrequency of small movements of expression, of natural blinking of swinging the arms in walking all small automatic movements, is such that the movement can be performed in full strength, if a voluntary effort is made The absence of such movements is related by the patient to a stiffness or feeling of resistance in the muscles even before such resistance can be felt by the physician When rigidity becomes palpable in the limbs the slowing and difficulty in voluntary acts become gradually more intense It is natural, therefore to relate the disorder of movement to the gradual development of a rigidity of the muscles with which it is coextensive in its later stages Occasionally however, slowness in initiating movement is extreme in the absence of palpable rigidity

Some evidence of the rigidity, if only the staring expression of the facies is always present, when the tremor is appreciable In other patients the rigidity is present for a time before tremor begins but persistent rigidity without any evidence of tremor always should lead to suspicion of arteriosclerotic or other lesion of the basal ganglia symptomatic parkinsonism

The rigidity when fully developed, is more apparent in the shoulder and hip muscles than in more distal joints It is present in all muscles acting at these joints although more intense in the flexor groups It early affects the flexors of the spine and of the neck inducing the characteristic huddled posture of these patients A relatively rapid passive extension of elbow or wrist will encounter some resistance which is felt throughout the passive movement It lacks the 'catch' or sudden maximum found in spasticity and is for this reason, called "plastic If tremor is present or about to develop, the passive relaxation of the muscle is felt to occur in a series of rhythmic steps each corresponding to a beat of the masked tremor cogwheel phenomenon In idiopathic paralysis agitans the rigidity is seldom intense and although beginning in the limbs of one side,

Retrocollic spasm extending the neck instead of the usual flexion always should suggest symptomatic parkinsonism although it has been described in the idiopathic condition as also has been described a tightly clenched hand[19 20] *Asymmetrical distortions are not a feature of the classical disease*

Sensory Disorders — Fleeting pains and aches in the limbs are common but are inconstant until severe immobilization has occurred They are thus associated with arthritic changes in the periarticular structures Sensory function is not disturbed otherwise by the disease A sense of internal heat or an intolerance of heat is not infrequent and is not accompanied by any actual change in temperature or by flushing Continual moisture of the skin may be associated with this sensation

Mental Functions — Intellectual function is not impaired The patient is however greatly fatigued by the incessant tremor throughout his waking hours so that, as the disease advances he reaches a state of persistent exhaustion with impaired initiative At this stage emotional disturbance is common and may take the form of severe depression Sands suggests that the disease appears commonly in stoical personalities who become complaining and querulous as a result *Throughout the course of the disease psychological factors certainly play* a prominent part in lessening or increasing the ability of the patient to combat disability and fatigue in greater measure than in most progressive diseases Loss of memory and other evidence of dementia indicate complicating factors In particular hallucinosis is a common reaction to the solanaceous drugs frequently used in treatment

Course

Sudden changes in the clinical course of the disease including sudden onset invariably are related to extrinsic factors the chief of which is the ill effects of emotional stress or grief which appear to lessen the ability of the patient to overcome his disability Injury to any part also hastens the course of the disease probably through the emotional shock entailed

Pathology

Reports of cases in which paralysis agitans was found to be related to gross *lesions of the brain are invariably unsatisfactory owing either to insufficiently* clear data as to the clinical state or to inability to exclude a chance coincidence of gross lesion in a disease with such chronic course The case with a cyst in the optic thalamus reported by Oppolzer in 1861[21] for example certainly was one of multiple sclerosis There is now general agreement that the characteristic disease has no pathology visible to the naked eye Nor have early reports of patho

dition is not a complete block of nervous function but a relative one It also raises the question as to whether the essential disturbance is not the weakness or lack of some *type of movement* All movements can be performed by voluntary effort, and Wilson [6] has shown clearly that true synergy, relationship between prime mover, antagonist fixator and cocontraction, is undisturbed, and that reciprocal innervation of antagonists still takes place In the present state of knowledge it is not possible to be sure, however, that movements ordinarily performed unconsciously, such as walking swallowing blinking are made only with conscious effort, because rigidity is impeding the normal automatic movement mechanism or because the normal automatic mechanism is itself weakened and is replaced by a voluntary imitation The occurrence of bilateral spasticity, as in pseudo bulbar palsy, however, also induces an expressionless facies with retracted upper eyelids and even a bodily posture that may closely imitate parkinsonism, although the hyperreflexia in mouth jaw and other parts clearly distinguishes the two Further Walshe[47] has shown that deafferentation of the muscles with novocain will abolish the rigidity, and previously slow movements then will be made rapidly The tremor is unaffected by this procedure Until more information is forthcoming the explanation of embarrassment of movement by rigidity and the occasional momentary suspension of rigidity by emotion accounts for most of the clinical behavior of the disorder

No derangement of either primary or discriminative *sensation* occurs in the course of the disease Further the *tendon reflexes*, although usually brisk in the early stages, do not show any change of pathological degree until the muscles concerned become so rigid that the muscle fibers cannot show the additional contraction The superficial reflexes, including the plantar responses, likewise are not altered *Control of the sphincters* is unaffected except where immobility finally induces incontinence, or where prostatic troubles are an independent complication

Gait and Posture — From what has been said of the rigidity associated with the disease it will be clear that a progressive flexion of the neck trunk and limbs occurs in its course The hands take up a characteristic posture of flexion of the metacarpo phalangeal joints with extension of the interphalangeal joints the thumb being held in opposition against the flexed first finger In many cases the hand closely resembles that of rheumatoid arthritis as first indicated by Ordenstein[76], and indeed rheumatoid changes may be present This, however, appears to be coincidence as are also the osteo arthritic changes commonly encountered in the shoulder joints These changes may be attributed to the secondary effects of prolonged immobilization in patients of advanced age Deformities of the feet usually are delayed until a late stage, when pes equinus with inversion occurs

description is in general terms Davison[1] reports on 8 cases including some already reported by the previous authors and was impressed by the greater involvement of the substantia nigra Two others of his cases had an onset at 22 and 25 years of age and one of these showed some Alzheimer cells The illustration of the supposed predominantly nigral changes in another case is not impressive Hallerworden[1] [1] claims that a fibrillary change in nerve cells precedes degeneration Newstaedter and Liber [2] review the pathology of the disease and confirm the general findings of Bielschowsky Degeneration of the pallidum was present in marked degree in all their cases Changes in the dentate and olivary nuclei were frequent and the substantia nigra unaffected in two Benda and Cobb[1] find difficulty in defining pathological evidence to differentiate paralysis agitans from post-encephalitic parkinsonism The changes in the post encephalitic syndrome will be discussed later It will be noted however that when cases of early onset slow course presence of torsion postures tremors of the head and unusual postures of the extremities are excluded the changes in the substantia nigra are insignificant compared with those in the globus pallidus On the other hand we are not convinced that the substantia nigra is ever entirely unaffected in true paralysis agitans

In no case has there been any evidence of causal agent either inflammatory or toxic or of closely related nutritional deficiency or glandular disease There is no evidence of associated disease of the liver

Most investigators agree with Jakob in characterizing the type of cell change as akin to senile involution The fatty degeneration of nerve cells is however found in such toxic conditions as the Korsakoff syndrome and pellagra and it must be admitted that a type of disturbance of neural metabolism may well underlie the condition It will be noted that the cellular disorder is widespread in extrapyramidal motor systems and is only relatively selective in incidence in the pallidum

Treatment

In the absence of any information as to the cause of the disease the treatment of paralysis agitans remains on a symptomatic basis As in all chronic disease states the first essential is the adjustment of the activities of the patient to the measure of his disability If it be borne in mind that every movement requires more than normal amount of exertion that true rest is impossible except in sleep a regime which husbands the patient s energies for essential purposes is the first requisite Regular exercise is essential but only a small proportion of this should be devoted to walking and a regular program of movements of all joints several times a day will greatly increase the comfort of the patient In early stages such exercises can be achieved by the patient himself In later phases of

logical changes in the muscles and spinal cord been sustained by modern methods of investigation

Manchot[77] in 1904 described all the essential pathological features including atrophy of pallidum and substantia nigra Jelgersma[8] in 1908 demonstrated paling of the medullated fibre systems of the ansa lenticularis and its contributions to the thalamus and Forel s field Lewy[79, 9, 93] stressed chronic cellular atrophy in the striatum and pallidum The Vogts[51] consider the loss of ground substance around the vessels, giving a moth eaten appearance etat crible characteristic although this is not always fully developed Arteriosclerotic and other vascular changes are inconstant and may be entirely absent in advanced states of the disease Tretiakoff[94] emphasized changes in the substantia nigra to which he and others have attached primary importance in the genesis of the motor symptoms

Bielschowsky[9] in a careful examination of 6 cases found clear evidence of cell loss in caudate nucleus, putamen and globus pallidus He insists that in true paralysis agitans the changes in striatum and pallidum are constant those in the substantia nigra inconstant Our own observations are in complete agreement Bielschowsky agrees with Lewy that the process is essentially a fatty and lipoidal degeneration affecting both large and small cell types and is more rapid in the pallidum with the appearance of greater amounts of extracellular free fat These changes are beautifully illustrated in Lewy's monograph[93] The process is associated with changes in the small blood vessels and capillaries leading to capillary fibrosis, which in turn gives the mottled appearance to the ground substance etat crible of the Vogts visible with simple stains such as Van Gieson Bielschowsky agreed with Spatz that calcium and iron deposits around the vessels result from abnormal nervous metabolism rather than primary vascular change The identical disease process often is widely evident in the cortex thalamus (ventrolateral nuclei), in the central grav substantia nigra substantia innominata pons and medulla His observations in cases of chronic chorea in which rigidity supervened and in which the pallidum was then recently affected, led him to identify the pallidal lesion as responsible for rigidity, but he will not further specify a clinico pathological correlati n L hermitte and Cornil[96] and Foix[97] had reached similar conclusions Jacob[98] reported similar findings with emphasis on the changes in large cells, which certainly show the degenerative change more clearly but with doubtful quantitative selective incidence Of the cases included by Keschner and Sloane[99], 1931 in their series one showed an etat marbre and cystic degeneration of one striatum as well as scattered but mild changes in the substantia nigra This is an unusual and possibly extreme example of glial reaction It was thought that the substantia nigra was more affected than the pallidum although etat cribre was present in the latter, and the

Progressive Atrophy of the Globus Pallidus

Synonyms —Paralysis agitans juvenilis familiaris juvenile paralysis agitans

Introduction

In 1910 Willige[108] reviewed a group of cases called juvenile paralysis agitans Of 14 such cases 6 were familial Ramsay Hunt in 1917 also gave an excellent review of previously recorded cases and added the autopsy findings in one case Four more familial cases had been recorded by 1917 Since that time a large number of cases of post encephalitic parkinsonism in childhood and adolescence and further knowledge of Wilson s disease have confused the clinical picture particularly since many of the clinical criteria are common to all these disorders The pathology of the condition however remains distinct and merits separate description

Since the age of onset may be in the third or fourth decade it is suggested that the adjective juvenile be dropped In Hunt s autopsied case the age of onset was 15 years and in his 3 other cases 13 years 26 years and 30 years In Van Bogaert s case [7] the symptoms commenced at the age of 7 years

Symptomatology

Besides the strong familial tendency of the disease the clinical state is distinguished from classical paralysis agitans by the early age of onset a slower progression of symptoms the comparatively early and severe involvement of the bulbar muscles the characteristic tremor is more extensive and severe and rigidity is more intense and subject to localized spasm

The disease makes its appearance in children or young people of normal intelligence as a tremor of the foot or hand of rhythmical type with increasing rigidity Spread of the affection to the other limbs occurs in about 5 years and is accompanied by severe impairment of articulation and deglutition At this stage there is usually tremor or nystagmus of the eyes accompanied by rhythmical twitches of the eyelids Great slowing and impairment of movements of the patient result

The tremor is more rapid 5 to 6 oscillations a second [4] than in paralysis agitans but in the fingers assumes the same characteristics except that it is intensified at the beginning of movement and damped a little at the end of movement At times the whole body shakes Rigidity eventually becomes extreme and even in early stages is associated with localized exaggerations such as torticollic spasm fixation of one hand in a fist with strongly adducted thumb (com

the disease an assistant will be required Light massage is of temporary benefit, but deep massage or electrical treatment is not helpful

In order to keep the tremor and rigidity at a minimum, tranquillity of mind is essential Many patients continue active occupations for several years after the onset of the disease by busying themselves with tasks within their limitations and by adherence to a regular schedule Exposure to cold increases the rigidity, but whereas the disability is less in a hot climate, the patient frequently finds high temperatures extremely uncomfortable owing to the sense of general warmth associated with the disease

The effect of hyoscine in lessening parkinsonian rigidity, first noticed by Gnauck in 1882, according to Mendel[69] is shared by all the solanaceous group of drugs (atropine, stramonium, hyoscyamus) In some cases there is also a notable effect in lessening tremor, but unfortunately this is exceptional The effect of these drugs is not appreciable until dosage is sufficient to produce their other physiological effects, namely the lessening of salivation and paralysis of accommodation of the eyes In patients, in whom drooling of saliva is troublesome the former side effect is an advantage otherwise it can, to some extent be overcome by the concurrent administration of pilocarpine nitrate, gr 1/5 (12 mgm), once or twice daily

Defect in accommodation is more difficult to compensate Instillation of eserine in the eye is troublesome, and some patients prefer to have compensating spectacles made

There is great variation of opinion as to the most effective solanaceous drug and the best mode of administration Atropine and hyoscyamus have a longer lasting effect on accommodation, and either hyoscine or stramonium is preferred There is no evidence that a combination is more effective than either singly and patients appear to derive some further benefit from a change from one to another after 6 to 12 months Hyoscine is given as the hydrobromide in small tablets by mouth beginning with gr 1/150 (0 4 mgm) three times a day and working up to gr 1/100 (0 6 mgm) or even gr 1/75 (0 9 mgm) at the same frequency Stramonium is given as tincture or liquid extract in dosage of 15 to 30 minims (1 2 to 1 8 c c) three times a day There is no evidence that special preparations of Bulgarian belladonna are more efficacious than active pharmacopeial tincture[1, 4, 105]

Treatment of paralysis agitans by solanaceous drugs is severely limited by the relatively reduced tolerance of such drugs in later life The large dosage that can be employed in post encephalitic parkinsonism (see in a later section) induces restlessness insomnia and states of confusion In such patients and indeed in the routine management of all advanced stages of the disease, a simple bromide sedative with barbiturate at night generally is more satisfactory

POST ENCEPHALITIC PARKINSONISM

Synonyms — Chronic epidemic encephalitis Von Economo s disease

Introduction

From 1916 to 1927 successive waves of epidemic encephalitis swept first Europe the United States (1918 onwards) the rest of America and then the remainder of the globe Sporadic cases continued as late as 1931 The distinctive features of this disease included a predilection of the virus for the immediate subthalamic region and midbrain with consequent appearance of parkinsonism either in the course of the initial acute illness or at an interval after the acute phase had passed Although other epidemics of encephalitis have been observed before and since none has had the same distressing sequel The subject has been reviewed ably by many authors of whom Wimmer[99] (1924) Hall[110] (1924) Economo[11] (1929) and Wilson[1] (1940) may be recommended particularly The two reports of the Matheson Commission[12 1] (1929 193) are excellent for statistics and bibliography Notable features are the extreme diversity of the immediate clinical symptomatology the rarity of case to case infection and the lack of success in isolation of the causal virus in spite of many attempts although some considered a neurotropic form of herpes virus to be the cause All age groups were affected We are here only concerned with the extrapyramidal sequelae

Symptomatology

Parkinsonism in the Phase of Acute Encephalitis — The initial illness in the epidemic period was usually a condition of lethargy or profound somnolence epidemic stupor' encephalitis lethargica associated with irregular fever and mild lymphocytosis in the spinal fluid The appearance of cranial nerve palsies particularly oculomotor paralysis was common Less commonly convulsions hemiplegia delirium punctuated the clinical course In the earlier epidemic waves myoclonus and hiccups were common In later series reversal of sleeping rhythm the somnolence appearing during the day and bizarre respiratory irregularities such as forced expiration were more frequent The duration of stupor and fever were extremely variable and in the light of the later appearance of mild sequelae it was evident that there had been many ambulatory and unrecognized cases

At any stage in the acute illness great slowing of movement associated with palpable rigidity in the limbs with or without the alternating tremors at rest

pare Hunt's illustration) Rigidity, although present, was always very mild in Van Bogaert's case

A very characteristic non familial case with onset at the age of 9 years is reported by Hall[10] The rapid parkinsonian tremor of the proximal segments of the limbs and of the head with rigidly flexed postures of the hands and feet and otherwise mild parkinsonian posture and expression are remarkable in their differences from paralysis agitans on the one hand and pseudosclerosis on the other

When paralysis agitans occurs in siblings late in life, the condition is characteristic of the usual presenile syndrome except for a certain 'fluidity' of tremor, *which involving the fingers one moment, passes imperceptibly* to the wrist in the next In a sister and brother reported by Wilson and observed by ourselves this feature was especially remarkable The tendency to fixed postures of the limbs and other features reported in the juvenile cases is, however, absent

Pathology

Unfortunately the brain has been studied in only two cases, that of Hunt and that of Van Bogaert[1 17] In neither was there any family history of the disease which began at the age of 15 years with death 25 years later in Hunt's case and began at the age of 7 years with death 23 years later in Van Bogaert's case[10] The outstanding finding was a degeneration of the nerve cells of the globus pallidus *on both sides of the brain in both cases with some slight affection of the* substantia nigra in Bogaert's patient In both the putamen caudatum and corpus Luysii were mildly affected There was no evidence of change other than simple neuronic atrophy with moderate increase of glia nuclei There was also no evidence of liver damage or of corneal pigmentation In view of the later maturation of conceptions of hepato lenticular degeneration (see in a subsequent section) *it is possible that some of the earlier recorded cases of familial* 'juvenile paralysis agitans' not proved by autopsy were in reality examples of pseudo sclerosis in view of the presence of coarse tremors increased by movement "nystagmus" and irregular spasms (compare case of Bonhoeffer, cited by Van Bogaert) The absence of liver damage and the type of simple glial proliferation, however set the two verified cases in the category of paralysis agitans *from which differentiation is possible only on clinical grounds*

demonstrable in the limbs Rigidity of the neck also was commonly prominent in a manner not seen in paralysis agitans

The course of the disorder also was notable Contrary to the tendency of paralysis agitans to progress steadily with perhaps occasional periods of apparent arrest the post encephalitic after either a steady or irregular progress for some months commonly reached a steadily maintained degree of disability which would persist for some years In some a steady lessening of disability would then occur and in a few cases a complete disappearance of symptoms Patients who recovered usually had suffered a mild degree of disorder at a long interval after the acute phase and the maximum duration of symptoms was in the neighborhood of one or two years The cases with severe disability of early onset usually remained severely incapacitated Early parkinsonism and rapid recovery were exceptional and the possibility of relapse in such an instance remained high More commonly a spontaneous improvement or disappearance of the rigidity and tremor was associated with the appearance of torticollis or other spasms or vice versa

The appearance of the symptoms was not associated with fever leucocytosis or changes in the spinal fluid or with any other factor except the psychological which could always produce remarkable transient changes and occasionally was correlated with a change in course Of the many varied clinical pictures one closely resembling paralysis agitans was the most common

Clinical Signs

The *tremor* is in a small group of cases absent for the whole course of the disease When present it is rhythmical and most prominent at rest as in paralysis agitans but differs in a faster rate 5 to 8 a second and a greater involvement of proximal joints wrist and elbow particularly often knee, shoulder and neck In children the rate is as fast as 9 a second [1] The faster rhythm is manifested generally by an abrupt jerking at times even violent alternation as compared with the soft gentle undulation of paralysis agitans Whether by reason of arrest in an early stage of unilateral development or by reason of great asymmetry in the proportion of tremor and rigidity the tremor is more often one sided for the whole course of the disease thus documenting an essential difference in the central lesions of the two diseases Tremor of the closed eyelids blepharoclonus was also more prominent and regularly observable

The *rigidity* is in most cases much more intense than in the presenile disease and remarkable in its asymmetry It could be limited to one side throughout the whole illness There is not only disproportion between the two sides of the body but also in one or other group of spinal muscles resulting in scoliosis torti

characteristic of parkinsonism, could appear The onset could be one sided or bilateral, insidious or abrupt associated with fever or in a completely afebrile stage Characteristic case histories are given by Tilney and Howe[11] and others The rigidity was plastic in character, usually mild in degree and without fixed attitudes except for a slight degree of flexion of limbs and spine and expressionless glassy staring facies even more remarkable than in presenile paralysis agitans The onset of either rigidity or tremor or both could be extremely abrupt after a fever had continued for several weeks as in a case related by Tilney and Howe[115] In cases where parkinsonism complicated the febrile stage, a fatal termination was common The parkinsonism otherwise usually persisted but in a few cases early recovery without further motor symptoms occurred Rigidity was more common than tremor In some cases fine tremors, increased by movement appeared In others myoclonus spasms akin to torsion spasm, choreic movements, tremors of the tongue and bizarre tics were seen[11 116]

Parkinsonism as an After effect of Encephalitis — In its most characteristic form the clinical evidence of damage to the basal ganglia and subthalamic nuclei appeared at an interval after the acute phase of the disease The interval varied greatly and could be as brief as a few days or as long as 20 years After long intervals of time the question of proof of relationship naturally arose In many cases there has been histological demonstration of persistent characteristic, inflammatory lesions, *where intervals of freedom from symptoms up to 4½ years* had occurred before the onset of parkinsonism To the clinician however, the symptomatology and clinical state had so many striking features not seen in association together in other states that the appearance of the patient was considered in itself pathognomonic Thus from 1930 to 1940 when many mild but characteristic clinical syndromes still were appearing frequently it was impossible to obtain any history of encephalitic illness The acute stage years earlier, had either not been recognized as such or the illness had been extremely slight or had been forgotten Occasionally the correctness of such clinical deduction was verified later by the discovery of an old clinical record of a brief illness in 1918–25 with diagnosis of 'epidemic stupor' or such revealing information

The parkinsonian aftermath was of gradual and insidious onset, hastened only by emotional crisis or accident as is paralysis agitans The first symptom was more often rigidity than tremor, and equally common as first sign was one or other of the spasmodic phenomena torticollis oculogyric crises etc, so prominent in this disease or in children, behavior disorder In any case the characteristic parkinsonian mask like stillness of facies would be noticed very early and often long before symptoms appeared This sign, omitted from Parkinson s original description of paralysis agitans was in fact much more prominent and consistent in the post encephalitic disorder, whether or not rigidity or tremor was

demonstrable in the limbs Rigidity of the neck also was commonly prominent in a manner not seen in paralysis agitans

The course of the disorder also was notable Contrary to the tendency of paralysis agitans to progress steadily with perhaps occasional periods of apparent arrest the post encephalitic after either a steady or irregular progress for some months commonly reached a steadily maintained degree of disability which would persist for some years In some a steady lessening of disability would then occur and in a few cases a complete disappearance of symptoms Patients who recovered usually had suffered a mild degree of disorder at a long interval after the acute phase and the maximum duration of symptoms was in the neighborhood of one or two years The cases with severe disability of early onset usually remained severely incapacitated Early parkinsonism and rapid recovery were exceptional and the possibility of relapse in such an instance remained high More commonly a spontaneous improvement or disappearance of the rigidity and tremor was associated with the appearance of torticollic or other spasms or vice versa

The appearance of the symptoms was not associated with fever leucocytosis or changes in the spinal fluid or with any other factor except the psychological which could always produce remarkable transient changes and occasionally was correlated with a change in course Of the many varied clinical pictures one closely resembling paralysis agitans was the most common

Clinical Signs

The *tremor* is in a small group of cases absent for the whole course of the disease When present it is rhythmical and most prominent at rest as in paralysis agitans but differs in a faster rate 5 to 8 a second and a greater involvement of proximal joints wrist and elbow particularly often knee shoulder and neck In children the rate is as fast as 9 a second The faster rhythm is manifested generally by an abrupt jerking at times even violent alternation as compared with the soft gentle undulation of paralysis agitans Whether by reason of arrest in an early stage of unilateral development or by reason of great asymmetry in the proportion of tremor and rigidity the tremor is more often one sided for the whole course of the disease thus documenting an essential difference in the central lesions of the two diseases Tremor of the closed eyelids blepharoclonus was also more prominent and regularly observable

The *rigidity* is in most cases much more intense than in the presenile disease and remarkable in its asymmetry It could be limited to one side throughout the whole illness There is not only disproportion between the two sides of the body but also in one or other group of spinal muscles resulting in scoliosis torti

collis, retrocollic spasm, torsion movements of the trunk and asymmetrical postures of the limbs in standing and walking Dysarthria was a prominent and early sign and difficulty in maintaining balance in turning or walking is evident at an earlier age Drooling of saliva owing to infrequency of swallowing is very common, although actual dysphagia is rare

Spasmodic Phenomena — A very characteristic feature, present in about 15 to 20 per cent of cases is the occurrence of *oculogyric crises* visual fits or oculogyric spasm These are spasms of deviation of the eyes of sudden onset and termination lasting for minutes or hours The most usual variety was an upward deviation, associated with raised eyelids in irregular flickering tremor, but lateral deviation to one side or convergent spasm occurs in some patients The deviation and type of spasm remained constant in the same patient The frequency of occurrence is irregular, from several in one day to intervals of weeks or months We have at present a patient under observation who has maintained a rate of one crisis every 7th to 8th day for 6 years The crisis begins in waking hours and sometimes is precipitated by a willed ocular movement in the same direction There is associated ache in the eyes or headache but no pain or other disorder In unusual cases a compulsive thought or obsession accompanies each crisis giving ground for much speculation as to the nature of the crisis or compulsive phenomena by various writers without however any clear conclusion Some of these compulsions were extremely complicated stereotyped movements or behavior They are discussed by von Economo[111] Some of the behavior disorder in children was strongly determined also by obsessive traits as for example a patient of ours whose only trouble was a penchant for stealing bicycles

In earlier years but still occurring sporadically there was seen a peculiar phenomenon allied to *tonic innervation* which itself also occurred as a rare variant The patient in walking flexed the hip on one side to a greater degree in successive steps so that after 20 to 100 paces the hip became acutely flexed on the abdomen and the gait brought to a standstill After a few moments the limb relaxed but the spasm was progressively renewed with further effort I have observed a similar progressive spasm of the extensors of the ankle (see Dystonia Musculorum later on in this chapter)

Spasmodic torticollis also occurs as a variant of the maintained variety but in our experience there was always a steady background of maintained torticollic spasm and evidence of parkinsonian rigidity

The *disturbance of speech* when severe, sometimes is accompanied by palilalia or echolalia, the tendency to repeat a word or phrase over and over with great rapidity and usually progressive inaudibility

No clear cut vasomotor or pilomotor disorder accompanies the disease, though a *hyperidrosis* or a greasy skin is common

The *reflexes* are unchanged except for the burial of tendon reflexes in muscular rigidity when that is intense If however the initial acute encephalitis had been severe signs of hemiparesis might remain as a stationary residual mark and in rare instances ocular palsy or epilepsy were similar sequelae, unaffected by the course of the parkinsonism Apart from the residua there is an almost constant *defect in convergence of the eyes* associated with defect in reaction of the pupil to accommodation reaction to light being unaffected These defects may be of any degree up to complete loss of these functions The *pupils* are unequal and irregular in a small proportion of cases

Although *delinquent behavior* was a more prominent symptom as a sequel to the acute illness in children usually there was some associated parkinsonian rigidity and posture The behavior disorder was not a progressive illness but like the parkinsonism tended to reach a stationary state from which improvement sometimes occurred after a long interval

The author has not seen an example of post encephalitic parkinsonism where that symptom had appeared since 1940 and knows of no instance of encephalitis *followed by parkinsonism since 1931 It is likely however that sporadic cases* may continue to occur for there is some evidence that the disease or one very similar had occurred long before 1915[111, 113, 115]

Pathology

In the initial stage of acute encephalitis perivascular lymphocytic infiltration was widespread in the cortex brain stem and spinal cord The greatest intensity however centered upon the midbrain where cell damage was present in all nuclei The appearance of parkinsonism as a symptom correlated with more severe damage to the substantia nigra (Lucksch and Spatz[1]) When parkinsonism had appeared recently as a sequel to the disease lymphocytic accumulations were present also strongly suggesting continued or renewed activity of the virus In late stages all evidence of inflammatory reaction had disappeared The constant and pathognomonic lesion in the nervous system is atrophy of the substantia nigra in the midbrain with great lessening of its pigmentation first noticed by Tretiakoff[94] Hohmann[118] Spatz[1, 9] Benda and Cobb and McAlpine Microscopically most of the nerve cells of the zona compacta and many of those in the zona reticulata have disappeared There is a mild diffuse glial reaction with granules of pigment either lying free or engulfed by phagocytic microglia In a large proportion of cases similar cell loss is found in the pallidum substantia innominata and locus cæruleus In other cases the cellular atrophy extends to the striatum and cortex but in no place is it as severe as in the substantia nigra The changes are seldom absolutely symmetrical and are more intense on the side

opposite to that showing greater rigidity in life Lymphocytic infiltration of perivascular spaces in the substantia nigra and any other affected parts persists as long as six years after the acute illness No essential change was noted in cases with tremor compared with those without

Nerve fibers and sheaths are unaffected except for some mild fiber loss in the ansa lenticularis, field of Forel and similar, clearly identified extrapyramidal pathways These appear to be only secondary to the cellular degeneration The disease does not attack myelin The etat fibreux and etat crible, so characteristic of paralysis agitans as also the fatty changes in remaining cells usually are absent, although this may be only an expression of shorter total duration Calcification or siderosis in the walls of small vessels in the basal ganglia is common in cases of long standing[1 0]

Treatment

Treatment of these conditions is as already outlined for paralysis agitans Patients with post encephalitic parkinsonism, being naturally younger and more disabled by rigidity derive more benefit from full dosage of drugs of the solanaceous group Psychological and emotional equilibrium is all important Since the rigidity and tremor tend to reach a stable and often localized state surgical measures for relief are worth discussion, particularly for tremor, which responds little if at all to medicinal treatment None however has been wholly satisfactory Section of the dorsal nerve roots or dorsal columns or anterolateral cordotomy is without effect on the tremor although diminishing rigidity slightly The relative value of other procedures is discussed at some length by Bucy[1 1], Klemme[1] , Meyers[1 3] and Putnam[1 4] in the Proceedings of the 1940 meeting of the Association for Research in Nervous and Mental Disease, with full bibliography Removal of the premotor cortex (area 6) has not been of any value in most hands Removal of area 8 (center for movement of eyes) was strikingly successful in a case of Poole[1] but not in other hands Removal of the head of the caudate nucleus diminished the tremor in some of Meyers cases with greater or complete loss of tremor when the anterior limb of the internal capsule is sectioned[1 3 1 4] Section of the ansa lenticularis by means of a special instrument and a difficult approach was claimed to be of great value by Meyers[1 3], but the high mortality appears prohibitive Pyramidal tract section in the high cervical region of the spinal cord was found by Putnam[1 4] to reduce tremor greatly with very little weakness in the limbs

None of these operative procedures is entirely satisfactory and the greatest success has always followed the production of hemiparesis As many including Parkinson have observed the tremor is abolished by the occurrence of hemi

plegia although recurring when voluntary movement recovers in more than moderate degree In patients desperately requiring relief from tremor a small *excision of area 4 and 6 for the limb concerned sparing some of area 4 deep in* the central sulcus appears to give a most satisfactory result[1] Such operative interference appears to have the greatest chance of success in young patients

Arteriosclerotic Parkinsonism

Introduction

The earlier writers refer frequently to paralysis agitans sine agitone Although rigidity without tremor is frequent as a sequel to epidemic encephalitis the most common other type consistently without tremor is that associated with cerebrovascular disease Indeed it is extremely uncommon for any form of involuntary movement tremor chorea or torsion spasms to be associated with vascular *lesions in the basal ganglia It is as if the ischemic process lacked some selec*tive process necessary to produce the characteristic tremor of paralysis agitans In the few cases where tremor was associated with proven vascular lesions there is always the doubt of possible co existence of true paralysis agitans of which the age distribution allows full overlap with that of cerebral arteriosclerosis

The disorder is not seen in young subjects suffering from malignant hypertension but appears usually in the sixth or seventh decade The considerable literature which has accumulated on the subject of arteriosclerotic parkinsonism has *been reviewed at length by Critchley [1] whose classification into five types is as* follows *Type 1* characterized by rigidity fixed facies and short stepping gait *Type 2* as type 1 with the addition of pseudo bulbar manifestations (dysarthria dysphagia spontaneous laughter and crying) with or without pyramidal disorder *Type 3* as type 1 but with the addition of dementia and incontinence of urine and feces *Type 4* as type 1 with signs of pyramidal disease but without pseudo bulbar manifestations (mixed pyramido pallidal syndrome) *Type 5* as type 1 but with the superimposition of cerebellar symptoms (mixed pallido-cerebellar syndrome)

The present author deprecates the extension of the appellation arteriosclerotic parkinsonism to cover the last groupings named above i e type 2 3 4 and 5 In the first place if fixity of facial expression and loss of other small expressive movements is attributable to hampering of movement by rigidity a similar fixity *of expression must be allowed to pseudo bulbar palsy Secondly if it be granted* that multiple vascular lesions may lead to parkinsonism the symptom may be expected to accompany many variations of generalized cerebrovascular disease We prefer therefore to restrict the term to the first type mentioned when parkin

sonism is alone or predominantly the clinical manifestation The milder forms of arteriosclerotic parkinsonism are those described by Marie[1 8] as ' lacunaires', the more severe forms those described by Foerster[1 9] as "arteriosclerotic rigidity '

Symptomatology

The onset seldom is abrupt and indeed is then open to suspicion of being true paralysis agitans, which has been provoked by crisis or emotional shock Most usually a progressive slowness in movement and fixity of posture are noticed first by friends or relatives The gait becomes slower, the steps shorter (' marche a petits pas ", Marie), and movement of the body as a whole on turning round is noticeable Festination and propulsion are rare, but there is early difficulty in walking down stairs, mainly, it appears, due to liability to lose balance, if the patient bends forward to look for the next step Forward flexion of the trunk and general flexion of the limbs are not as evident as in paralysis agitans It is unusual for there to be any mental enfeeblement or disturbance of control of the sphincters, and if these are present, the possibility that disturbance of gait is arising as a result of an apraxia always comes up for consideration and is difficult to exclude

On examination the characteristic resistance to passive movement is felt in the muscles It is more evident in the lower limbs than the upper and may be more appreciable on one side The fixity of facies is present but may not be remarkable in degree at a stage when walking is clearly impaired The upper lids are retracted, and speech is slurred or slowed or both The absence of tremor is notable

Rapidly alternating movements are hampered by the rigidity even in the upper limbs where the rigidity may be palpable only with difficulty The handwriting consequently tends to become smaller but lacks the tremulousness seen in paralysis agitans The reflexes are not altered in an uncomplicated case, but the tendon jerks commonly are more brisk than usual, unless they are hampered by the rigidity Reflex grasping reflex sucking and other release phenomena associated with diffuse lesions of the frontal cortex and pseudobulbar palsy are lacking The muscles may feel abnormally hard on palpation, particularly in the lower limbs

Cardiovascular hypertension is the rule and usually is far advanced when the disorder of movement becomes manifest but some cases show little evidence of peripheral vascular disease[130] Signs of renal damage often are minimal or even absent The disorder is slowly progressive over a number of years and usually is terminated by other complications of hypertension

Pathology

The most common finding is a diffuse distribution throughout the external capsule striatum and pallidum of small lacunes or foci of softening each 1 to 3 mm in extent and golden yellowish in color There is extensive loss of cells both in striatum and pallidum with a pronounced degree of glial proliferation Recent perivascular hemorrhages may be present and the iron pigment in the older lesions is evidence of their having been primarily hemorrhagic Atherosclerosis is present in the blood vessels of the basal ganglia besides calcification which is in any case frequent in these vessels after middle life (Hurst [32]) Similar disease of the substantia nigra may be present but is not constant The lacunar lesions may be widespread involving the cortex and cerebral white matter indiscriminately but dementia with pseudobulbar and other spastic changes are then likely The lacunar state may occur predominantly in the caudate nucleus and putamen with little or no evidence of parkinsonism It is therefore likely that the pallidal lesions are those usually responsible for the syndrome

Treatment

Besides the general measures for alleviation of cardiovascular hypertensive disease and the use of exercises mentioned for paralysis agitans no particular treatment is advised Drugs of the solanaceous group (hyoscine stramonium etc) usually are not tolerated in sufficient dosage to lessen the rigidity Courses of iodides have been found beneficial to some patients

Syphilitic Parkinsonism

The occurrence of parkinsonian tremor in patients who have symptoms or signs of tabes dorsalis has been commented upon by many writers under various names such as syphilitic paralysis agitans mesencephalitis syphilitica (Wilson and Cobb[13] and Wohlfahrt[1]) The possibility of coincidence is clearly recognized by Wilson [34] In autopsied cases an etat lacunaire has been found in some again also a coincidence The case of Mella and Katz[133] was a man aged 45 year with a history of parkinsonian tremor for 3 years and tabetic signs for a longer period Autopsy revealed loss of cells in the globus pallidus with perivascular lymphocytic accumulations but no true luetic endarteritis Instances of choreic movement or torsion spasm accompanying a frank chronic syphilitic meningitis have been observed and in a case reported by myself the movements subsided with treatment Fixed facies and general posture is frequently observed also in the course of general paresis and can be correlated with the presence of changes

in the lenticular nuclei, but this again hardly merits the name syphilitic parkinsonism. True parkinsonism attributable to syphilitic disease is, therefore, an unproven entity.

Parkinsonism Following Intoxications

Carbon Monoxide Poisoning

Parkinsonism following carbon monoxide poisoning is extremely unusual, but a number of cases is now on record. Exposure to the gas may have been in any of a variety of ways but most frequently, from the accidental or suicidal inhalation of coal gas or the exhaust gas of internal combustion engines. Rare cases result from exposure in coal mines especially after explosions. Parkinsonism appears as an after effect of severe and critical poisoning and is associated with severe apathy, defect in memory and change in personality. In the early stages of recovery from coma, choreic or myoclonic movements are not infrequent. The immobility of apathy passes gradually into a true parkinsonian rigidity and fixity of posture after an interval of usually 2 to 4 weeks (Nielson and Ingham[136], Grinker[137], Shillito and associates[138]), and this condition then progresses to reach a stationary stage after some months. Nielson[139] reports a case in which subsequent recovery occurred after a mild degree of rigidity. In others a considerably longer interval of one or more years occurred between the intoxication and the first appearance of parkinsonian symptoms[140]. The possibility of other cause for such parkinsonism then arises, but Raskin and Mullaney reported a case, subsequently analyzed by Alexander[141] with further data, where rhythmic tremors of the lips, later of the upper limbs, associated with parkinsonian rigidity appeared 6 years after the carbon monoxide intoxication. Compulsive phenomena reminiscent of post encephalitic parkinsonism occurred. Yet at autopsy 15 years after intoxication the characteristic lesions of the pallidum were present. Memory defect and change in character had been continuous throughout the illness, and it seems as Bumke and Krapf assert in their review[14], the latent interval is not one of freedom from symptoms, an important point in prognosis. Other patients present evidence of focal cortical damage, such as aphasia, apraxia, agnosia or even spinal cord lesions with or without parkinsonism and these symptoms also may appear or worsen after a "latent interval."

Pathology.—A very characteristic softening of the anterior (rostral) portion of the pallidum on both sides is found commonly in patients who have survived 24 hours or more after severe CO poisoning. The softened area may vary in extent on the two sides as in Grinker's case[137] with correspondingly more severe rigidity on the side opposite the larger lesion. The neighboring internal capsule may be involved. These lesions usually are associated with a large number of

small areas of demyelination scattered throughout both hemispheres and even larger areas of softening in the cortex The process behaves as does any ischemic softening with eventual gliosis In early cases there is some evidence of softening of different ages in different areas but in the case of Alexander[141] the histology offered no explanation of the long latent interval The smaller vessels show degenerative changes and in the acute stages irregular dilatations and ring hemorrhages[141] In some cases brain purpura has been reported There is no evidence that carbon monoxide has a selective effect for the nervous parenchyma of the pallidum An apparently identical pallidal lesion is produced by manganese cyanide nitrous oxide or carbon dioxide poisoning but with much less regularity[14] The areas of softening in carbon monoxide poisoning may spare the pallidum also or in addition involve areas of cortex or brain stem [43] It is therefore possible that the common pallidal lesions are due to a combination of two factors first anoxia which is less specific when acting alone and second the longer persistence of the gas carbon monoxide in the center of solid organs after a certain critical concentration has been reached The immediate cause of the softenings appears to be explained best by damage to vascular endothelium Chronic poisoning has to be taken into account also for Lewey and Drabkin[14] recently have reported cortical and pallidal necrosis in dogs subjected to repeated exposure to a concentration of 0 01 volume per cent CO which led to approximately 20 per cent HbCO

Manganese Intoxication

Workers with manganese powder unless protected from inhalation develop a severe parkinsonian rigidity with slowing of speech after some months of exposure The rigidity affects the trunk as well as the limbs and facies Rhythmical tremors of the head and proximal parts of the limbs are common although the pill rolling movements of the hands do not occur Severe cases are described by Charles[1] who notes some improvement after treatment with raw liver An inversion deformity of the feet was present Twitching of muscles in the limbs and torticollis have been described European writers[1 1] refer to a manganese stutter as a characteristic speech which however is not noted by Charles or Gayle[147] Change in personality euphoria and emotional lability are usual The condition improves to some degree after removal from further ingestion of the manganese dust The industrial hazards are discussed by Edsall Wilbur and Drinker[148] Voss[14] reports cases resembling pseudobulbar and bulbar paralysis rather than parkinsonism

Pathology — Symmetrical atrophy of the globus pallidus and caudate nucleus with less conspicuous changes in the putamen thalamus and cortex are described in a case carefully investigated by Canavan and associates[1 0] There is also an

in the lenticular nuclei but this again hardly merits the name syphilitic parkinsonism True parkinsonism attributable to syphilitic disease is, therefore, an unproven entity

Parkinsonism Following Intoxications

Carbon Monoxide Poisoning

Parkinsonism following carbon monoxide poisoning is extremely unusual but a number of cases is now on record Exposure to the gas may have been in any of a variety of ways but most frequently, from the accidental or suicidal inhalation of coal gas or the exhaust gas of internal combustion engines Rare cases result from exposure in coal mines especially after explosions Parkinsonism appears as an after effect of severe and critical poisoning and is associated with severe apathy, defect in memory and change in personality In the early stages of recovery from coma, choreic or myoclonic movements are not infrequent The immobility of apathy passes gradually into a true parkinsonian rigidity and fixity of posture after an interval of usually 2 to 4 weeks (Nielson and Ingham[114], Grinker[137], Shillito and associates[138]), and this condition then progresses to reach a stationary stage after some months Nielson[139] reports a case in which subsequent recovery occurred after a mild degree of rigidity In others a considerably longer interval of one or more years occurred between the intoxication and the first appearance of parkinsonian symptoms[140] The possibility of other cause for such parkinsonism then arises but Raskin and Mullaney reported a case subsequently analyzed by Alexander[141] with further data where rhythmic tremors of the lips later of the upper limbs associated with parkinsonian rigidity appeared 6 years after the carbon monoxide intoxication Compulsive phenomena reminiscent of post encephalitic parkinsonism occurred Yet at autopsy 15 years after intoxication the characteristic lesions of the pallidum were present Memory defect and change in character had been continuous throughout the illness and it seems, as Bumke and Krapf assert in their review[142] the latent interval is not one of freedom from symptoms an important point in prognosis Other patients present evidence of focal cortical damage such as aphasia, apraxia, agnosia or even spinal cord lesions with or without parkinsonism, and these symptoms also may appear or worsen after a 'latent interval'

Pathology —A very characteristic softening of the anterior (rostral) portion of the pallidum on both sides is found commonly in patients who have survived 24 hours or more after severe CO poisoning The softened area may vary in extent on the two sides as in Grinker s case[137] with correspondingly more severe rigidity on the side opposite the larger lesion The neighboring internal capsule may be involved These lesions usually are associated with a large number of

Hepato Lenticular Degeneration

Synonyms — Progressive lenticular degeneration or Wilson's disease pseudo sclerosis (Westphal Strumpell disease)

Definition and Incidence

Hepato lenticular degeneration is a familial disease in which cirrhosis of the liver is associated with the occurrence of progressive tremor or rigidity and usually both The rigidity has the plastic quality associated with other diseases of the basal ganglia and is characterized further by asymmetry and variability in the resulting postures The tremor is particular in its absence in complete relaxation and its increase in amplitude in certain types of movement or posture Choreo athetoid movements may rarely replace the tremor The most obvious pathology in the central nervous system in rapidly progressive cases is a bilateral softening of the lenticular nucleus particularly the putamen but this is but the focus of a widespread disorder of nervous structure associated with a special type of glial proliferation The cirrhosis is coarsely nodular comparable to that following subacute yellow atrophy and is associated with the appearance of a characteristic pigmentation of the cornea and occasionally of the skin

The disease is more common than generally believed for many of the milder forms, and certainly a great many of the cases dying in the first stage are unrecognized There are now over 150 cases recorded in the literature Of 111 cases *analyzed by Luthy*[159] *68 were males 43 were females The age of onset of nervous* symptoms most usually is between the ages of 11 and 25 The earliest onsets on record are at the ages of 4 years[1] and 7 years[18] The latest onsets were at the ages of 40 years[6] and 41 years[1,3] The extremes of duration of the disease are from one month in a very acute case[164] to 43 years[1,9]

Historical

Up to the beginning of the present century a heterogeneous series of disorders of bodily posture associated with involuntary movements remained poorly differentiated from diseases such as chorea paralysis agitans and multiple sclerosis and from each other The differentiation of the group about to be described was a gradual process In 1883 Westphal[165] described in two patients a nervous disorder characterized by tremors difficulty in speech and slowness in movement with rigidity but without nystagmus He did not find any changes in the brain and there is no mention of cirrhosis of the liver although the organ is said to have been congested and yellow in color in the second case He was concerned chiefly

associated cirrhosis of the liver Cerebral lesions and subacute hepatitis were reproduced experimentally in monkeys by Mella[1 1] Damaged nerve cells became first swollen, often vacuolated and later, pyknotic Neuronophagia was associated with mild gliosis There was no vascular damage The changes pictured are not very convincing The Hursts[16] failed to produce any central nervous lesion in rabbits or guinea pigs although very severe cirrhosis resulted

Other Intoxications Cyanide Carbon Disulfide Mercury Anoxia

Carbon disulfide (Negro[1 3] and others) has been described as the cause of parkinsonism and cyanide has been shown to produce necrosis of the pallidum[154] These conditions are, however, rare compared with the other manifestations of intoxications with these substances It has been suggested that the rhythmical tremor of mercury poisoning and the occasional occurrence of choreiform movements is related to parkinsonism in spite of worsening of the tremor by muscular contraction The facies and lingual tremor of these patients certainly are suggestive of parkinsonism The pathology of the condition is however, unknown

Parkinsonian syndromes have resulted from anoxia during nitrous oxide anesthesia with necrosis of the outer pallidum and with some months delay in the appearance of rigidity in one case (Courville[15]) or with choreic movements[156] but are unusual symptoms of this condition as of other kinds of anoxia

Familial and Senile Tremor

A familial liability to tremor of the hands on movement or in sustained posture but not at rest is a relatively common disorder A number of pedigrees is recorded by Kreiss[1 7], who notes its benign course The tremor is rhythmical but irregular in amplitude and is often mistaken for alcoholic tremor, which it closely resembles There is no associated rigidity or change in posture The prominence of the tremor in the fingers affects the handwriting Many patients can momentarily control the tremor for some delicate manual operation Thus, it can be compatible with skilled manual occupations The tremor usually first appears in adolescence and then remains stationary for many years perhaps a lifetime It is however in no way different from senile tremor and in severe degree is accompanied by the rhythmical side to side shaking of the head characteristic of that condition[158] Either type may occur without family history Although there is no direct relationship with parkinsonism the latter disease occasionally occurs in families liable to familial tremor[73] The pathology of the condition is unknown although resemblance to degeneration of the red nucleus suggests an aplasia of that structure Alcohol has a very deleterious effect and should be avoided

uable details from the still existent records of the cases of Gowers and Ormerod he says little of "pseudo sclerosis" which is mentioned only in an "addendum" (p 508) in which he remarks on the description by Fleischer (1909) and Volsch (1911) of cases of pseudosclerosis with cirrhosis of the liver without abnormality of the brain Wilson believed that these cases belonged to the category of progressive lenticular degeneration In subsequent works Wilson always maintained that the "features . . . once imagined to distinguish pseudosclerosis are now seen to be valueless . . . and that . . . there is far more valid reason to include any cases so termed *and having* . . . cirrhotic lesions of the liver under the class of lenticular degeneration (a definite morbid entity)" (Posthumous text *Neurology*[112])

The unhappy name "pseudo sclerosis" nevertheless is descriptive of a condition which considerably differed from that described by Wilson and described hardly at all in the English literature (Holloway 1914 Thomas 1917[1] autopsy in neither case) Whereas distorted postures were a prominent feature of Wilson s cases tremor with little or no postural aberration was the outstanding characteristic of "pseudo sclerosis" Further whereas softening or cavitation of the lenticular nucleus was an obvious feature of progressive lenticular degeneration case after case of pseudosclerosis had been reported without any such change Wilson attempted to explain the absence of lenticular degeneration in the cases of Gowers and Volsch by lack of histological examination absence of "sufficient information" or the brief course of the disease The degeneration in his own cases was however visible to the naked eye and the course of "pseudo sclerosis" usually is much longer than that of progressive lenticular degeneration In 1912 Hosslin and Alzheimer demonstrated the remarkable disorder of the cerebral glia which underlies "pseudo sclerosis" and soon was confirmed by others Hall (1921) in reporting a transitional case where both the widespread Alzheimer glial changes and lenticular softening of Wilson were present and pointing to a similar case earlier described by Stocker[1] . . . admirably reviewed [8] the whole subject and now bridged the gap between the two dissimilar entities

A further important feature had been established already for the paper by Fleischer [7] in 1909 mentioned as an afterthought by Wilson was in fact the confirmation by autopsy that a curious ring of golden corneal pigmentation and cirrhosis of the liver were both associated with pseudosclerosis In 1912 Fleischer[179] published a further report on 3 autopsied cases including one in which the corneal pigmentation had been first described by Kayser in 1902 and thought by him to be suffering from multiple sclerosis Fleischer was unable to find evidence of cerebral pathology although Spielmeyer later (1920) described[18] the glial changes of Alzheimer in the sections of one of his cases Pollock [81] in 1917 described the corneal pigmentation in Wilson s progressive lenticular degeneration

with differentiation from multiple sclerosis and apologetically proposed the term "pseudosclerosis" Further similar cases were described by Strumpell[1 6 16], his last case showing early cirrhosis of the liver, to which he did not attach any particular importance There was no hint of familial incidence Although neither author could demonstrate cerebral pathology, each was convinced that the disorder was not hysteria, then claiming much attention Similarities with diffuse sclerosis and hereditary syphilis were discussed

Meanwhile isolated instances of another syndrome had been described briefly by Gowers[16] in 1888 under the name "tetanoid chorea A familial, acute, progressive nervous illness at an early age was described where a generalized tonic spasm of extension of the limbs was associated with fixity of smiling facial expression The flexed fingers 'at times were extended and slowly moved in the irregular way characteristic of athetosis' There was a persistent pyrexia No abnormality of the brain was found, and a cirrhosis of the liver, although present was not mentioned until a later account in 1906 Homen[163] in 1890 and 1892 reported a family with a similar disease but with tremor instead of athetosis and associated with bilateral softenings of the lenticular nuclei and cirrhosis of the liver, which he attributed to hereditary syphilis Ormerod[1 0] in 1890 reported a case of a boy of 10 years with symptoms closely resembling those of Homen's patients and with identical pathological findings, and he stressed the relationship to cirrhosis of the liver for the first time Physicians interested in diseases of the liver also had noticed instances of the coincidence of nervous disorder with hepatic cirrhosis in young people without however attaching any importance to the association[13 1 9] So far these various clinical categories had remained without correlation with morbid nervous anatomy except for the observation of degeneration of the lenticular nuclei in their cases by Homen and Ormerod, cited as a curiosity by the one and as evidence of hereditary syphilis by the other

The years 1908 to 1912 are remarkable for advances in the neuropathology of diseases of the basal ganglia but none can compare with the contribution of Kinnier Wilson[13], first read to the Neurological Society of London in 1911 and published in 1912 under the title Progressive Lenticular Degeneration A Familial Nervous Disease Associated with Cirrhosis of the Liver In it he brought together the descriptions of Gowers, Ormerod and Homen and 4 further cases of the disorder in 3 of which detailed post mortem examination had been made He established "a definite symptom complex, whose chief features are generalized tremor dysarthria and dysphagia, muscular rigidity and hypertonicity, emaciation, spasmodic contractions contractures emotionalism" "In pure cases the affection constitutes an extrapyramidal motor disease, for the reflexes are normal

Although Wilson considered previously described cases at length adding val

progressive lenticular degeneration also was familial it was not associated with jaundice or other abnormality at birth and was progressive and never congenital There is no evidence of any underlying blood dyscrasia except for a hemorrhagic diathesis with fall in platelets in late stages and secondary to the splenic hypertrophy The nature of the cirrhosis indicates the intermittent action of some toxin possibly related to some unrecognized inborn errors of metabolism such as cystinuria porphyria or gout Nor is there any lipoidal accumulation resembling Niemann Pick s disease The absence of any cerebral degeneration or corneal pigmentation in Laennec s cirrhosis or hemochromatosis indicates that the underlying disorder in hepato lenticular degeneration is highly specific

Symptomatology

Hepatic Symptoms — As has been indicated above the essential basis of the disease is a progressive subacute hepatitis leading to a coarsely nodular cirrhosis of the liver In his original monograph Wilson stated the cirrhosis rarely if ever gave rise to symptoms during life While this has been true of many cases and obvious signs of portal obstruction such as ascites and hematemesis usually are completely absent there is commonly a history of recurrent mild hepatic disorder The first case of Wilson had had jaundice 4 years before the onset of nervous symptoms his fourth case an attack 3½ years before with apparent recovery in the interval in both Such outspoken attacks are unusual More commonly the prodromal signs are only interpreted as hepatic disease when the history is viewed in retrospect Thus patients will give a history of recurrent indigestion associated with mild fever subcostal pain or tenderness and in severe attacks perhaps a mild icterus preceding the first nervous symptoms by some 2 or 3 years Nausea and vomiting usually are the most prominent symptoms in these attacks although diarrhea occurs in some Nearer the onset of the first nervous symptoms perhaps over the preceding 6 to 12 months a liability to recurrent headache with listlessness and anorexia make their appearance In the family reported by Barnes and Hurst[1] these prodromata were unusually pronounced and in 2 of the 4 members ascites and hematemesis occurred before the onset of nervous symptoms Several families are on record now in which some members have succumbed to hepatic cirrhosis before the development of nervous symptoms The use of the term abdominal Wilson [7] for such cases has little to commend it In some patients this first stage the hepatic phase is entirely symptomless and the nervous signs appear in association with similar minor symptomatology It is extremely rare for nervous symptoms long to precede these minor hepatic symptoms After the appearance of nervous symptoms the second stage of Luthy ascites and hematemesis have occurred in a number of cases The

and its appearance before the nervous symptoms in some cases The pigmentation Kayser Fleischer ring has been recognized since the monograph by Hall as a certain diagnostic feature found in no other nervous disease

An additional clinical syndrome torsion spasm has been allied with progressive lenticular degeneration and pseudosclerosis since the report of the case of Thomalla[18], shown by Bielschowsky[183] to have cirrhosis and lenticular softenings Similar cases have been reported by Wimmer[184 18], Spiller[1 6] and others and now are included under the comprehensive term "hepato lenticular' degeneration proposed by Hall[109]

Since that time the most valuable single contribution is that of Luthy[1 9], who besides providing an excellent review described a case of extreme duration and established certain changes in the later evolution of the disorder in patients who survive, indicating a tendency for a late stage resembling 'pseudo sclerosis" to be derived from an earlier rigid variety

Etiology

The disease is strongly familial, 96 cases having occurred in 34 families, compared with 13 isolated cases[18] No clear case of direct inheritance of the disease is on record, although 2 of Hall s cases were related through unaffected mother and maternal grandfather with two affected uncles De Lisi[188] reports 2 cases having a common great grandfather As Hall[108] indicates, such a pedigree requires the coincidence of two recessive factors to explain the disease In Wilson s fourth case there is a family history of hepatic disorder in two previous generations but no autopsy proof was obtained Similarly there was a history of death of the father of the patients of L hermitte and Muncie[180] from " multiple sclerosis' Negative family histories in the previous generations are obtained commonly Kehrer[187] and Wilson[173] have drawn attention to the tendency of affected families to be large, an average of 7 births in 49 mothers Goodhart and Balser[184] record cases in twins The affected patients may be early or late in a large family

Autopsy records show that the cirrhosis invariably is present before nervous symptoms occur The cause of each is unknown There is no evidence of the action of an infective agent and now no question of intoxication by manganese or other metals such as silver or copper previously suspected on account of the corneal pigmentation The corneal pigmentation is absent in other kinds of cirrhosis There is no evidence of blood dyscrasia except for a hemorrhagic diathesis in late stages and resulting from the cirrhosis and splenic hypertrophy

Wilson[13] drew attention to the known damage to the basal ganglia in icterus gravis neonatorum and the strongly familial nature of that affection now known to be traceable to Rh incompatibility in parents He pointed out that, although

frequently to an ease of laughter that is pathological usually a short loud rire spasmodique at the slightest event Pathological crying is seen sometimes There is no difficulty in vision and the patient may spend a great part of the time reading Sooner or later usually within 12 months of the first appearance of stiffness of the limbs the posture of the hands becomes altered with a tendency to hold the arms flexed the wrists flexed to a right angle with the forearm the fingers half extended The knee is held semiflexed the foot inverted These postures usually are asymmetrical After some months some contracture results so that it is difficult to extend the elbow and wrist fully The tremor is now con stant in wrist and elbow in knee ankle and toes and at times in the jaw All voluntary movement is slowed greatly and is accompanied by great intensifica tion of the tremor In this advanced stage of the disease there is usually some evidence of defect in memory and in some cases behavior disorder of a mild kind is prominent There is no evidence of impairment of control of the sphincters until such disability and enfeeblement have occurred as to account for occasional incontinence

Throughout the course of development of the nervous symptoms dysarthria and dysphagia are prominent in all types of progressive lenticular degeneration In addition a number of patients have been described in whom bizarre move ments are superimposed on a state basically resembling that described above In Hall s first case[1] the tremor and rigidity progressed for 2 years from the age of 25 when a rigidity of the tongue was first noted In the next 3 years the tongue became habitually protruded to the left in association with lateral flexion of the neck to the left and a strange attitude of the arms The whole attitude main tained for hours at a time could from time to time relax into one of general mild rigidity and tremor only to be renewed with any attempt to move or speak In a similar case cited by Hall his case 6 spasms of the neck and difficulty in speech began at the age of 13 years and gradually became more intense and less inter mittent In a spasm the tongue was held strongly against the palate At rest mild rigidity was apparent and slight tremors appeared before his death at the age of 19 years This dystonic attitude was clearly most developed in the patient of Thomalla a boy of 13 years who developed rigidity of the right arm and leg which soon was accompanied by difficulty in speech and swallowing and twist ing movements of the trunk without tremor leading to death about 9 months from the onset

At the other end of the scale the complaint can be solely of tremor In such cases of pseudo sclerosis the onset usually is after the age of o and the course more benign In a patient under our care the onset was relatively sudden at the age of 23 with increasing tremor of both upper limbs for 4 weeks following which it remained stationary for 3 years In the fourth year it gradually worsened

degree of liability to evidence of portal obstruction appears to vary from family to family

In some patients the terminal event is a febrile delirium with vomiting with or without ascites and subicteric tinge, passing into hepatic coma as in case 3 of Barnes and Hurst[191] In case 4 of the same authors such a termination was accompanied by the first nervous manifestations

The appearance of crops of purpuric spots with some swelling of the joints was noted in Wilson s sixth case and several times since The condition is attributed to the gross enlargement of the spleen in such cases and is associated with fall in blood platelets, leukopenia, more or less severe anemia and other evidence of the hemorrhagic diathesis

Nervous Symptoms —As the brief historical account given above has indicated the clinical picture of hepato lenticular degeneration grew from the recognition of two different states the ' pseudo sclerosis ' of Westphal Strumpell, Fleischer and Alzheimer and the ' progressive lenticular degeneration ' of Wilson, to which later was added a certain variety of ' torsion spasm " by Thomalla and Bielschowsky The same disease has therefore differing clinical manifestations depending upon the variable proportion of mobile spasm and rigidity on the one hand torsion spasm ' when uncomplicated, and tremor, ' pseudo sclerosis ' on the other A large intermediate group of patients with both tremor and abnormal postures are characteristic of the cases originally brought together by Wilson We shall here deal primarily with the general and best known type and differentiate the others in subsequent sections

The onset of nervous symptoms usually is insidious and appears in the form of a fine tremor of the hands The tremor is often a little worse in one hand than in the other and interferes particularly with handwriting and carrying food to the mouth It is periodic, being at first noticeable under stress or excitement, and disappears in complete repose At almost the same time, or a little later a change in speech is noticed words are slurred and the patient tends to keep the mouth open The tremor and dysarthria in most cases slowly increase in the following months and soon are associated with some difficulty in walking The difficulty is related to the appearance of stiffness in one or both lower limbs and in some patients to the extension of tremor to these limbs At this stage the patient may be very restless and unable to settle at anything As the tremors and stiffness develop the difficulty in articulation becomes gradually severe and is associated with some difficulty in swallowing Saliva is more apt to drool from the almost continuously open mouth The expression becomes one of a fixed vacuous smile which together with the disordered speech and drooling may give a false impression of loss of intelligence

A degree of euphoria may be observed now varying from a tendency to smile

in the substance of the cornea near the cone The only other conditions resembling the Kayser Fleischer ring are the pigmentation of argyria and of Addison s disease In the former the pigment is conjunctival and brownish black in the latter the brownish pigment occasionally may extend onto the cornea[1 7] but it is then in the superficial corneal epithelium

In some patients symmetrical brownish pigmentation of the skin of the face neck and extremities has been noted (Fleischer Luthy) but only after the disease has existed for 10 years or more There may be large irregular cafe au lait patches on the back buttocks or other parts

Liver and Spleen — In the first purely hepatic stage of the disease the liver frequently is found to be enlarged in mild to moderate degree with hard firm border The spleen is palpable and in some cases greatly enlarged At least 4 cases are on record where the spleen was removed under the mistaken impression that the condition was Banti s disease [13] The occurrence of periods of low fever with vomiting sometimes diarrhea and rarely icterus has been referred to above The liver further is enlarged and frequently tender to palpation in these Frank ascites and edema of the ankles may be present

In the second stage of nervous symptomatology the liver usually is no longer palpable and liver dullness is diminished The spleen continues slowly to enlarge but seldom to very great proportions Ascites and signs of enlargement of the portal collateral circulation are very seldom conspicuous Luthy observes that the hepatic disorder may in fact recede with the appearance of nervous symptoms Jaundice certainly is less commonly reported in the second stage The present writer would rather put it that those patients with the longest course seldom present outspoken signs of portal obstruction at any time whereas those with frank signs in the first stage most usually present a rapidly progressive course in both hepatic and nervous symptoms in the second stage Attacks of jaundice in the second stage are extremely rare but febrile attacks may continue for 6 years or more as in Hall s first patient If splenomegaly is pronounced a mild secondary anemia is to be expected together with leukopenia low platelet count prolonged bleeding time and attacks of purpura More commonly there is no alteration of the blood count

Other Somatic Changes — Gastric analysis reveals no constant abnormality hypo or an acidity being recorded in some cases hyperacidity in others The stools are not in any way peculiar and the digestive process is little if at all disturbed Urobilin is commonly although not constantly increased in the urine up to 70 mgm or more in 24 hours compared with 20 mgm in the normal Glycosuria has been recorded frequently but was mild and not progressive and has been absent in most cases Vasomotor disorder is rarely present and then only as a mild acrocyanosis Osteoporosis has been found in a few instances No

then again to become stationary. As in the rigid patients the tremor is seen chiefly on movement and thus interferes with writing and eating. Dysarthria and dysphagia are minimal in degree and may not be complained of by the patient.

A sudden onset of tremor may follow a shock or injury or occur without cor relation with any other event. A transient but sudden stiffness of one side of the body has been reported as an early symptom in a few cases. Spontaneous fracture of a bone has occurred in at least 4 cases and was a first sign of the disease in Economo's patient[19]. Acrocyanosis has been noted in 6 of 111 cases by Luthy[159].

Physical Signs

Kayser Fleischer Ring. — The one certain unequivocal and unmistakable sign of this disease is the zone of golden brown pigmentation near the outer margin of the cornea, called the *Kayser Fleischer ring* (Fig. 2). It is not always present but appears sooner or later in the more chronic forms of the malady. Hall[16] notes that of 25 proven cases, in which the presence of the ring was specifically sought, it was found to be present in all of 16 instances of "pseudo sclerosis" and in 4 of 9 cases of 'progressive lenticular degeneration'. Frequently it is present before the onset of nervous symptoms and has never been found in the proven absence of cirrhosis. It is not found in any other form of nervous disease.

The Kayser Fleischer ring is seen best by oblique illumination, for it has a slight fluorescent or "smoky" appearance. In some lights it has a greenish tinge but by daylight is seen as a golden brown haze, which forms a band or zone 1 to 4 mm. wide separated from the limbus or margin of the cornea by a clear zone about 1 mm. in width. Its forward edge is ill defined, for it fades gradually into the central cornea. In earliest development I have found it only above and below and absent in the temporal and nasal margins. It is, therefore, most clearly seen in looking from above on the brightly illuminated eye (Fig. 2), the upper lid being retracted and the patient directed to look downwards; then it appears as a smoky golden brown haze. It is seen more easily if the iris is grey or grey green and may pass unnoticed if the iris is brown as for example in the illustration of Barnes and Hurst. The pigment is in the inner lining of the cornea, Descemet's membrane, and slit lamp examination clearly demonstrates this location. We have not encountered an instance of demonstration of its presence by slit lamp when it was not also clearly demonstrable by observation from above.

The Kayser Fleischer ring is not to be confused with another form of pigmentation described by Fleischer in the condition of "conical cornea", then occurring

in the substance [illegible]
the Kayser-Fleischer [illegible]
ease. In [illegible]
the brownish pigment [illegible]
in the [illegible]

In some patients [illegible]
neck and extremities [illegible]
ease has ex[illegible]
patches on the [illegible]

Liver and Spleen. — In [illegible]
frequently is [illegible]
border. The spleen [illegible]
cases are on record where [illegible]
that the condition was [illegible]
fever with vomiting, sometimes [illegible]
above. The liver further [illegible]
Frank ascites and edema [illegible]

In the second stage [illegible]
palpable and liver dullness is diminished. [illegible]
but seldom to very great proportions. [illegible]
portal collateral circulation are [illegible]
the hepatic disorder may in fact [illegible]
Jaundice certainly is less commonly [illegible]
writer would rather put it tha[illegible]
present outspoken signs of portal [illegible]
frank [illegible] in the first stage most usually [illegible]
both hepatic and nervous symptoms [illegible]
the second stage are extremely [illegible]
or [illegible] Hall's first patient [illegible]
[illegible] be expected together [illegible]
bleeding time and attacks of purpura. [illegible]
the [illegible]

Other Somatic Changes. — Ga[illegible]
hypo- or an-acidity being recorded [illegible]
stools are [illegible] in any way peculiar and the [illegible]
turbed. [illegible] is commonly a[illegible]
up to [illegible] or more in 24 hours [illegible]
cosuria has been recorded frequently [illegible]
been absent in most cases. Vasomotor [illegible]
as a mild acrocyanosis. Osteoporosis has been [illegible]

then again to become stationary As in the rigid patients the tremor is seen chiefly on movement and thus interferes with writing and eating Dysarthria and dysphagia are minimal in degree and may not be complained of by the patient

A sudden onset of tremor may follow a shock or injury or occur without correlation with any other event A transient but sudden stiffness of one side of the body has been reported as an early symptom in a few cases Spontaneous fracture of a bone has occurred in at least 4 cases and was a first sign of the disease in Economo s patient[19] Acrocyanosis has been noted in 6 of 111 cases by Luthy[1 9]

Physical Signs

Kayser Fleischer Ring — The one certain unequivocal and unmistakable sign of this disease is the zone of golden brown pigmentation near the outer margin of the cornea called the *Kayser Fleischer ring* (Fig 2) It is not always present but appears sooner or later in the more chronic forms of the malady Hall[1] notes that of 25 proven cases in which the presence of the ring was specifically sought it was found to be present in all of 16 instances of " pseudo sclerosis and in 4 of 9 cases of ' progressive lenticular degeneration Frequently it is present before the onset of nervous symptoms and has never been found in the proven absence of cirrhosis It is not found in any other form of nervous disease

The Kayser Fleischer ring is seen best by oblique illumination for it has a slight fluorescent or " smoky ' appearance In some lights it has a greenish tinge but by daylight is seen as a golden brown haze which forms a band or zone 1 to 4 mm wide separated from the limbus or margin of the cornea by a clear zone about 1 mm in width Its forward edge is ill defined, for it fades gradually into the central cornea In earliest development I have found it only above and below and absent in the temporal and nasal margins It is, therefore, most clearly seen in looking from above on the brightly illuminated eye (Fig 2) the upper lid being retracted and the patient directed to look downwards then it appears as a smoky golden brown haze It is seen more easily if the iris is grey or grey green, and may pass unnoticed if the iris is brown as for example in the illustration of Barnes and Hurst The pigment is in the inner lining of the cornea Descemet s membrane and slit lamp examination clearly demonstrates this location We have not encountered an instance of demonstration of its presence by slit lamp when it was not also clearly demonstrable by observation from above

The Kayser Fleischer ring is not to be confused with another form of pigmentation described by Fleischer in the condition of " conical cornea ', then occurring

variation in the general aspect of the patient *In the type of the disease called pseudo sclerosis* rigidity is inconspicuous and generally noticeable only in a certain fixity of expression usually not sufficiently maintained or constant to be comparable to the mask of parkinsonism Slight scoliosis or torticollis or both and mild pes cavus may be the only certain signs of true fixity of posture Passive movement of a joint during tremor at that joint elicits a rhythmical relaxation of muscles due to the contractile beats of the tremor While this is called cog wheel relaxation by some it is not the same phenomenon as the steps of relaxation of a true cogwheel rigidity Hunt[10] described hypotonia with intense tremor in one such case In such patients dysarthria and dysphagia are absent or minimal and the open mouth so typical of Wilson s disease is completely lacking

In the type of progressive lenticular degeneration muscular rigidity is early in appearance and may be the first sign of the disease It is responsible for the very characteristic appearance and posture of Wilson s cases All movement is greatly slowed the facial expression fixed in a smile the mouth open and saliva drools from the lips The limbs are held semi flexed in late stages with marked flexion of the wrists Passive movement encounters a soft yielding plastic resistance chiefly in the flexors of the limbs but also in extensors If tremor is present the relaxation is step like cogwheel A slurring dysarthria with monotonous lack of variation in timbre and particular difficulty in the enunciation of consonants is present from an early stage and progresses to complete anarthria Difficulty in swallowing accompanies the difficulty in speech The tongue palate and vocal cords appear to move slowly and with some limitation in amplitude The tongue sometimes appears fixed to the roof of the mouth by spasm Movements of the eyes are not usually affected although some patients have complained of diplopia in an early stage probably due to defect in convergence In later stages movements of the eyes are slowed or limited It is unusual for upward movement to be restricted as reported by Bridgman and Smyth[1] In Economo s patient rigidity became generalized and intense after an onset with dysarthria and difficulty in walking No tremor or involuntary movements appeared at any time but the plantar responses were extensor In other cases the characteristic tremor is superimposed on the rigidity The rigidity is not symmetrical being more evident in the limbs of one side than the other with corresponding slight or severe torticollis or scoliosis owing to unilateral preponderance of spinal rigidity There is frequently some difficulty in relaxing a grasp on the most severely affected hand

Dystonia — In many cases of Wilson s type there is added to the general rigidity a periodic distortion of head and limbs which is peculiar for each patient These bizarre postures are well seen in the illustrations of two of Hall s patients

endocrine disorder is regularly present, and such signs as are found indicate mild hypogonadism

The nervous symptoms may consist of various combinations of tremor, rigidity and dystonic postures These are of the general character of striatal symptoms but in addition changes in the deep reflexes and extensor plantar response are present in some few instances Choreoathetosis and athetosis have been described[11] but are unusual

Tremor — The most striking and most constant single symptom is the tremor This is seen most characteristically as a rhythmical flexion extension at the wrist joints when the arm is stretched out This is the "wing beating' (flugelschlagen) tremor of Strumpell[10a] It is irregular in amplitude in early development Its appearance in the wrists is in obvious contrast to the finger tremor of paralysis agitans In later development it involves the elbows and shoulders, then knee ankle and toes The fingers may become involved at any stage and in a small proportion of cases are the first to show the tremor, which may develop finger by finger The movement at the shoulder is also characteristic in being an alternating adduction abduction thus causing a flapping movement of the half adducted arms, swinging movement of Strumpell

The tremor is further peculiar among all other extrapyramidal disease in being absent in complete repose and increased by movement In finger to nose test the tremor is either slightly increased as the finger approaches the nose or becomes very violent In the latter case the violence appears to derive from the addition of the characteristic shoulder tremor as the arm is retracted at the shoulder Thus, the tremor is mildly increased by movement but greatly increased in certain postures of which extension of the wrist and elbow and lateral abduction at the shoulder are examples In this way the effect of movement is different from cerebellar or intention" tremor which is produced more directly by movement and of which the postural elements are seen only in the trunk as titubation In hepato lenticular degeneration the tremor does not involve the head or trunk until a very late stage The tongue may show one or two beats of the tremor during protrusion but not when at rest or when fully protruded

The rhythm usually is a little more rapid than in paralysis agitans, being 4 to 6 beats a second as compared with 3 to 5 in the latter disease At first it is fine in amplitude but an occasional beat of coarser amplitude soon appears A strong muscular contraction for example a hand grip, increases the tremor to some degree, but if the grip is maintained the tremor of the hand and fingers lessens commonly then overflowing' to elbow, shoulder or lower limb 'mobile tremor' In later stages bouts of tremor may shake the patient from time to time a perfect riot of tremulous movements' (Wilson)

Rigidity — The degree of muscular rigidity varies greatly with corresponding

lability commonly appears to impair judgment In most cases some evidence of mild dementia is present memory is inaccurate judgment poor and comprehension impaired in some degree This disturbance appears after the nervous symptoms and progresses slowly In some few patients usually those with a late onset of the disease[175 194] this mental change develops into a severe psychosis in which paranoid symptoms hallucinations and delusions of grandeur are described In a number of cases feeblemindedness has characterized the family before the onset of the disease This was so in a family observed by me and reported by Mc Ardle[100], and here as in others the condition was inborn and stationary and had no clear relationship to hepato lenticular degeneration

Convulsive Disorder — In several cases in the literature epileptiform attacks have been described These appear to have been recurrent tetanic spasms lasting a few minutes and are manifested in the terminal stages They are not clearly epileptic and indeed Barnes and Hurst[1] in describing such spasms in three of their patients liken them to tetanus for intense rigidity was accompanied by a risus sardonicus was provoked by stimulation and appeared to be painful Such bouts of severe rigidity generally have been called *striate epilepsy* when consciousness is not lost[1] Some have described transient hemi rigidity as an early sign of the disease Inconstancy appears to be a peculiarity of the rigidity as indeed of all dystonia Isolated syncopal attacks occur but are extremely rare In Hadfield s case [1] tetanic spasms were prominent but definite status epilepticus finally supervened before death The pathology in this patient was seen chiefly in the frontal cortex The spasms also are present in cases without obvious cortical damage Jacksonian or ordinary epilepsy is excessively rare in this disease The *electroencephalogram* does not reveal any abnormality in the early stages of the disease and only when the patient is considerably disabled by motor disturbance are changes regularly found[19 19] The disorder then takes the form of generalized slowing of rhythm Short runs of large slow waves closely resembling some types of convulsive disorder appear on the hemi phere opposite the sudden convulsive spasms when these occur The absence of any focal localization for such waves probably indicates a striatal origin especially since in Bridgman and Smyth s case[1] no focal cortical degeneration was found

Sensation and Reflexes — Hyperesthesia has been observed in one case In all others disorder of sensation has been absent in spite of the later changes in the thalamus in some of these Hyperreflexia with ankle clonus and an extensor plantar response occurred in about one sixth of these patients (Hall) Spastic paralysis is unknown These mild changes presumably are related to the mild involvement of the internal capsule by the nervous lesion True motor paralysis is not described Pathological laughing and crying resembling p eudobulbar phenomena are seen in a few patients and probably are due to bilateral damage

(I and VI), in each of whom the head was held turned to one side with the tongue rigidly held applied to the roof of the mouth or protruded to one side and with a distorted asymmetrical position of the upper limbs, one retracted at the shoulder, the other adducted close to the chest The fingers are hyperextended in the attitude common in the course of athetosis The abnormal posture is maintained for minutes or hours at a time then suddenly lapses leaving the patient with a simple general rigidity Any attempt to speak or move results in renewed spasm In such cases athetoid movements of the fingers frequently occur independently Such intermittent spasms are referred to by some as "athetosis of the proximal joints

After a survey of the literature one is impressed with the frequency with which the clinical phenomena can be divided into (1) a state of mild constant rigidity with tremor and (2) a superadded periodic spasm The spasm may be momentary, last minutes or hours or be continuous except for occasional brief lapses It is this inconstant, lapsing, quality of the spasm which distinguishes progressive lenticular degeneration from other striatal diseases, although some of the phenomena of post encephalitic parkinsonism closely resemble it Thus the ' tetanoid chorea of Gowers was described in the following words ' When told to shut his mouth, the patient used to push the lower jaw up with his hand, then the spasm of the muscles would seem to give way and he would close his mouth easily but it returned to the widely open position in a minute or so occasionally the patient could utter words or sentences more distinctly especially in the morning (reference no 13 p 302) Hadfield [91] notes that his patient did not appear particularly rigid until spoken to, when abruptly all the limbs forcibly flexed and adducted with spasm of the face and almost complete anarthria lasting some minutes Thus even the characteristic Wilsonian posture, the ' silly smile the open mouth the forced position of the tongue and the overflexed wrists, may itself lapse for lesser or greater periods of time or can have periodic mobile torsion spasms superadded All movements disappear in sleep with the exception of mild athetosis of the fingers in some severely affected patients

Torsion Spasm — In some patients the combination of asymmetrical spinal rigidity with mobile spasm results in torsion of the trunk and neck in a manner closely resembling dystonia musculorum deformans[18 184 186] Dysarthria is present from the onset a feature which occurs only very late in the course of the latter disease, where the early onset of severe lumbothoracic lordosis is also more prominent Such cases would cause less confusion if called "Wilson s disease with dystonia

Mental Status — In the later stages of the disease profound dysarthria and motor disability make it difficult for the patient to communicate his thoughts to others although he retains a lively interest in his surroundings Emotional

lability commonly appears to impair judgment. In most cases some evidence of mild dementia is present: memory is inaccurate, judgment poor and comprehension impaired in some degree. This disturbance appears after the nervous symptoms and progresses slowly. In some few patients, usually those with a late onset of the disease[17, 194, 19], this mental change develops into a severe psychosis in which paranoid symptoms, hallucinations and delusions of grandeur are described. In a number of cases feeblemindedness has characterized the family before the onset of the disease. This was so in a family observed by me and reported by McArdle[1, 6] and here as in others the condition was inborn and stationary and had no clear relationship to hepato-lenticular degeneration.

Convulsive Disorder. — In several cases in the literature epileptiform attacks have been described. These appear to have been recurrent tetanic spasms lasting a few minutes and are manifested in the terminal stages. They are not clearly epileptic and indeed Barnes and Hurst [1] in describing such spasms in three of their patients liken them to tetanus, for intense rigidity was accompanied by a risus sardonicus, was provoked by stimulation and appeared to be painful. Such bouts of severe rigidity generally have been called *striate epilepsy* when consciousness is not lost[197]. Some have described transient hemi-rigidity as an early sign of the disease. Inconstancy appears to be a peculiarity of the rigidity as indeed of all dystonia. Isolated syncopal attacks occur but are extremely rare. In Hadfield's case [1] tetanic spasms were prominent but definite status epilepticus finally supervened before death. The pathology in this patient was seen chiefly in the frontal cortex. The spasms also are present in cases without obvious cortical damage. Jacksonian or ordinary epilepsy is excessively rare in this disease. The *electroencephalogram* does not reveal any abnormality in the early stages of the disease and only when the patient is considerably disabled by motor disturbance are changes regularly found[194, 199]. The disorder then takes the form of generalized slowing of rhythm. Short runs of large slow waves closely resembling some types of convulsive disorder appear on the hemisphere opposite the sudden convulsive spasms when these occur. The absence of any focal localization for such waves probably indicates a striatal origin, especially since in Bridgman and Smyth's case[199] no focal cortical degeneration was found.

Sensation and Reflexes. — Hyperesthesia has been observed in one case. In all others disorder of sensation has been absent in spite of the later changes in the thalamus in some of these. Hyperreflexia with ankle clonus and an extensor plantar response occurred *in about one sixth of these patients (Hall). Spastic* paralysis is unknown. These mild changes presumably are related to the mild involvement of the internal capsule by the nervous lesion. True motor paralysis is not described. Pathological laughing and crying resembling pseudobulbar phenomena are seen in a few patients and probably are due to bilateral damage

to the genu of the internal capsule Reflex sucking and grasping are seen seldom and when present, probably have the same causation

Laboratory Data

The cerebrospinal fluid usually is normal in pressure and content of cells protein, globulin sugar and chlorides A mild pleocytosis has been noted in a very few cases possibly due to some extraneous pathology for one of these cases[1] suffered from terminal tuberculosis A mild increase in globulin has been recorded in a few other instances

Attempts to demonstrate the disorder in hepatic function have suffered from lack of tests of adequate sensitivity Urobilin or urobilinogen rarely are present in the urine although Hall found the former in 3 of his cases Even in cases such as those of Barnes and Hurst, where cirrhosis and toxic hepatic symptoms were prominent, these substances were not present in the urine in the intervals between attacks of hepatitis Levulose tolerance ammonia coefficient hemoclastic crisis and van den Bergh tests were negative also unless an episode of hepatitis happened to be present

Sweet, Gray and Allen[200] have carried out more sensitive tests of liver function in a series of 9 cases They found that the serum colloidal gold test of Gray prothrombin time and bilirubin excretion test are more sensitive than galactose tolerance bromsulphthalein retention or hippuric acid tests The plasma protein level and cholesterol ester partition proved to be of little or no value In our own cases the prothrombin time and colloidal gold test gave negative results whereas the cephalin flocculation test gave a positive result in 3 cases and later negative results in 2 of these all 3 of pseudosclerotic type

It appears that particularly in the pseudosclerotic type of the disease, the hepatic disorder is periodic and associated with very complete intermediate regeneration More success is likely to attend a test which would reveal the margin of detoxication possessed by the liver Such a test, however risks precipitation of a further crisis Attention therefore has been directed to the demonstration of embarrassment of the portal circulation for example by radiological demonstration of esophageal varices These too have given disappointing results in early stages of the disease when the information is particularly desired

In case of doubt, therefore, a liver biopsy may be justified and has been performed on many cases A local anesthetic should be used for these patients for they do not tolerate general anesthesia

As has been maintained earlier the blood count platelet count and bleeding time may be altered when hepatic damage is severe and gross splenomegaly is present, but usually not without purpuric indications

Pathology

Liver —The liver presents a nodular cirrhosis of variable degree The most usual finding is a shrunken firm liver with irregularly nodular surface The capsule is not thickened or adherent to surrounding structures In section nodules of varying size are found throughout the liver substance The size of the nodules varies from case to case depending on the chronicity of the condition In some early acute cases as Barnes and Hurst s[191] first case the nodules are uniformly small, 1 to 4 mm in diameter More usually the larger nodules are 1 to cm in diameter (Fig 2) and even larger The nodules are separated by bands of pink 1 h gray or white connective tissue 1 to 3 mm wide (Fig 2) The liver substance usually is distinctly jaundiced and some nodules are intensely fatty If the hepatic disorder had been terminally active fatty degeneration may be general Fibrous tissue rarely penetrates into the lobule the center of which is free from pathological fibrosis Microscopic examination reveals that in some lobules almost every cell is fat laden some greatly distended The nuclei of the liver cells often are two or three times normal diameter some pale some darker than normal and some pyknotic Around the central veins smaller cells with much smaller darkly staining nuclei are found and sometimes two nuclei within one cell Many cells contain a greenish brown pigment Very few contain bile pigment and granules which give an iron reaction are scarce both in Kupfer and in liver cells The capillaries are engorged and small bile ducts are frequent sometimes giving evidence of proliferation The fibrous tissue is relatively non cellular and usually contains sparse collections of round lymphocytic cells which also in places infiltrate small areas of necrosis of central hepatic cells The condition is the multiple nodular hyperplasia of Marchand the toxic cirrhosis of Mallory or the healed *yellow atrophy of other authors It may vary in degree from changes typical of* subacute hepatitis to a chronic stage where degeneration is found only at the periphery of the lobule and the fibrous septa do not show any sign of chronic inflammation Such cases usually give evidence of considerable portal obstruction a feature denied by the earlier writers

Spleen —The spleen varies greatly in size from case to case but usually is enlarged to some degree and shows evidence of marked congestion of some duration with corresponding degree of fibrosis

Cornea —Section of the cornea reveals that the Kayser Fleischer ring is due to the presence of dark brown pigment in the form of exceedingly fine granules in the lining cells of Descemet s membrane close to the basement membrane of these flat cells They are not present in parts of the eye other than where the ring is seen The solubilities of these granules as given by Hall and by Barnes and Hurst indicate that in spite of small divergences in solubilities found in different

cases the pigment is not any normal body pigment or any pigment found in the commoner pathological conditions It does not contain iron, does not color with stains for lipoid does not give the reactions of silver or manganese and is related most closely to malarial pigment i e a hematogenous pigment of unknown origin The location form and color of the pigmentation of the skin, meninges and kidneys of some cases on histochemical analysis have given reactions closely resembling those of argyria[1 2] The possibility of silver medication common at one time for multiple sclerosis, has seldom been excluded with certainty Although the nature of the pigment is unknown, it is certainly different from hemochromatosis

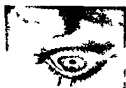
Brain — The changes in the brain are striking in the rigid types of the disease progressive lenticular degeneration consisting of symmetrical softenings often cystic cavitation centering on the putamen in the lenticular nucleus In the "pseudo sclerosis" type no change may be discerned by naked eye inspection of the brain and the unique alteration in the glia is seen only with the microscope Transitional cases are reported[1 1 8 128] The cirrhosis is the same in both conditions and is clearly the primary process, not only because hepatic symptoms often precede nervous symptoms but some members of families affected by the disease have succumbed to the cirrhosis without any demonstrable change in the brain (Barnes and Hurst[191] case IV) or with only the earliest sign of the gliosis of Alzheimer (case III of the same authors and others)

In the progressive lenticular degeneration as described by Wilson[13] in his first cases a cavity with irregular brownish colored lining and trebeculae replaced the posterior four fifths of the putamen and all the outer part of the globus pallidus The outer wall of the cavity had eroded the external capsule and claustrum and interiorly had damaged the genu and anterior limb of the internal capsule The caudate nuclei were greatly shrunken but preserved their general structure There was no change in the thalamus or other part In his third case Wilson found the posterior two thirds of the putamen on each side discolored friable somewhat shrunken and pitted with small holes The degenerated areas also included the middle third of the external capsule The globus pallidus was somewhat shrunken on each side but the caudate nucleus and thalamus appeared intact

Either of these changes cavitation or softening, centering on the lenticular nuclei have now been described in a large number of cases presenting the postures and rigidities described by Wilson and typical of the more rapidly progressive forms of hepato lenticular degeneration beginning in childhood or adolescence The softened area is often described as dark brownish or even brick red in color In Economo s case presenting extreme rigidity without tremor, the softenings involved the head of the caudate nucleus as well as the putamen[19] In the very rapidly progressive case of Howard and Royce (age 12 years duration 5½ weeks)

HEPATO-LENTICULAR DEGENERATION

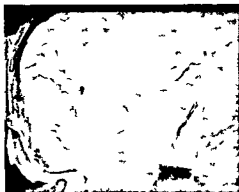


Kayser-Fleischer Ring



Liver- Gross Appearance



Liver on Section

FIG 2

there were also softenings in the thalamus red nucleus and internal capsule[1, 4] In some cases similar softenings have been found in the cerebral cortex involving the white matter and to a lesser extent the grey of several convolutions In one of Spielmeyer s cases the occipital lobes were affected[1, 9] in others[201, 191, 161] a symmetrical prefrontal area The cortical changes in some[201, 1, 1] were more severe than those in the lenticular nucleus The softenings were associated with exten sive formation of additional capillary vessels accompanied by the typical glial changes Smaller foci of similar damage were present in other parts of the cortex Hypermyelination may occur in similar patchy areas of the cortex[1, 9]

Microscopical examination reveals that the walls of the cavitation and the softened areas are extremely cellular Few if any recognizable nerve cells re main and these in the last stage of degeneration Large numbers of fat granule cells are present in areas of recent degeneration Most of the glial cells appear to have pale swollen cytoplasm with nuclear alterations varying from pyknotic changes in some to swelling and deformity in others A large pale nucleus with rounded cytoplasm difficult to stain by the Nissl method is very common There is a striking scarcity of neuroglia fibers The capillary vessels are in creased in number and often show bodies that give an iron reaction in their walls The large vessels show no changes except for some hyaline degeneration in the walls of vessels related directly to cavitation Perivascular collections of fat granule cells usually are present varying in quantity with the rapidity of the ill ness In the portions of the lenticular nucleus which have escaped softening most of the smaller nerve cells and many of the larger usually have disappeared The remainder show excentricity of nucleus and are shrunken with mulberry shaped nucleoli Satellitosis is common Glial increase is prominent Similar changes to a much less degree affect the nerve cells in the pallidum few if any of which appear normal and neuroglia is more extensive than usual The large cells of the caudate nucleus are similarly abnormal and actual loss of cells is as great as in the pallidum Changes of similar kind usually affect a number of nerve cells in the corpus subthalamicum and the dentate nucleus thalamus and the cerebral cortex particularly frontal cortex and pons Cavitation has been found in the dentate and pontine nuclei The substantia nigra usually is not affected

The myelinated fibers traversing the globus pallidus the ansa lenticularis and the lenticular fasciculus together with the fibers traversing the subthalamic nucleus are degenerated or in process of disintegration as Wilson described

It will at once be clear that the morbid process is widespread within the brain and that the peculiar localization of symmetrical softening in the lenticular nucleus is so to speak a focus of the disorder which not only effects other struc tures but may have other foci in addition No case has been described where the foci were elsewhere and the lenticular nucleus not at all affected Further it

should be clear that the softening and cavitation are not primarily related to gross vascular disease. Nor are the nerve cells of the lenticular nucleus primarily susceptible as a whole for portions may be relatively spared.

The type of case called "pseudo sclerosis" is particularly instructive. Here softening and cavitation usually are absent, although the lenticular nucleus is often dark in color and shrunken. In some cases it may be difficult to discern any certain macroscopic abnormality as in the first case of this kind described by Hosslin and Alzheimer[1.6]. The outlines of the basal ganglia and external capsule perhaps are not as distinct as usual. Microscopic examination reveals widespread evidence of damage to nerve cells in the basal ganglia and to a less degree in the cerebral cortex. In addition larger, special, neurological cells (Alzheimer type II cells) are found widely disseminated throughout the central nervous system with the exception of the spinal cord and in some cases the cerebellum. These cells have large pale nuclei 2 or 3 times the size of the nucleus of a normal astrocyte with weakly staining and comparatively scanty cytoplasm, usually without neuroglial fibers. The cytoplasm can best be stained with fuchsin light green. In some parts of the brain most commonly in the region of the external capsule but in some cases only in the pons[1.9] or red and dentate nuclei[1.4] or other structure, some glial cells are even larger and have 2 or 3 large pale and irregularly lobulated nuclei within one large protoplasmic mass. These are the "giant neuroglial cells" of Alzheimer (Alzheimer type I cells) and were found widely disseminated throughout the basal ganglia, the hypothalamus, pons and dentate nucleus in his first case. Wherever these abnormal glial cells are present in greatest number, the nerve cells show regressive and degenerative changes. The remaining glia is proliferated also in the most affected regions and may have undergone fibrous changes in the region of the putamen. Since Hall pointed out the essential identity of the two conditions many cases have been described when both cavitation and Alzheimer's glial changes are present. There is now little doubt that the histological appearance varies with the time and intensity of action of the noxa.

Any changes in blood vessels are considered to be entirely secondary to the neuroglial alterations. Alzheimer likened the giant glia cells to those found in tuberose sclerosis, and Bielschowsky[183] suggests that they are a blastomatous formation for this reason. The fourth case of Barnes and Hurst[181], when the patient died with the onset of nervous symptoms and no neuroglial or nerve cell changes had yet occurred demonstrated that the essential glial change develops with the disease. These investigators found intermediate stages in development of the large and giant glial cells from swollen astrocytes and demonstrated that they still possessed faintly staining fibers (Victoria blue method) attached to blood vessels. By following progressive degenerative changes in the chromatin they claim that the swollen cell is in a process of involution and finally disintegrates

In their third case the destructive changes were most marked in frontal cortex and putamen with lesser changes in the pallidum caudate nucleus and thalamus and no other change except for the presence of occasional Alzheimer cells in the mid brain In long standing cases of late onset the whole brain becomes greatly shrunken although the general nervous architecture is undisturbed The great est atrophy and reactive gliosis are found in the regions where softenings and cavitation occur in the more rapid syndromes of adolescence The essential morbid process is however a generalized cerebral disease

Borderline States (Marginal Syndromes)

Demole and Redalie [ ] reported in 19 2 2 patients with strong alcoholic his tory The first at the age of 46 developed besides clinical evidence of cirrhosis and alcoholic psychosis a marked postural tremor of all four extremities ab ent in complete repose and associated with a progre sive rigidity of all four limbs This patient was found at autopsy to have lenticular softenings and widespread Alzheimer II gliosis A second patient developed a similar clinical picture at the age of 60 and at autopsy had similar wide pread gliosis of the whole brain without softenings Van Werkom [ ] earlier had reported 2 similar cases about the age of 50 with predominantly mental symptoms and hepatic cirrhosis later tremor and rigidity He found characteri tic pathology of hepato lenticular degeneration in one In the other case the characteristic glial change was found with a hard sm oth liver No corneal pigmentation was noted in any of these cases Economo a d Schilder described a presenile syndrome strongly resembling late pseudo sclerosis with slight cirrhotic changes in the liver but without any of the charac teri tic changes in the brain In view of the establi hment of late pseudo sclerosis [ ] it appears clearly possible that many non familial examples of hepato lenticular degeneration may occur late in life or be facilitated in develop ment by alcoholism

Pathogenesis

The relationship between liver and brain is of particular interest not only be cau e of the enigma of hepato lenticular degeneration but for the possible light its solution may shed on paralysis agitans Huntington s chorea Hallervorden Spatz disease and a dozen other degenerative conditions which although not related to cirrhosis may well have a similar relationship to disordered metabolism As has been indicated above the hepatic cirrhosis precedes the nervous degeneration in hepato lenticular degeneration Although Levi described parkinsonism en countered in the course of more ordinary forms of cirrhosis of the liver such cases usually can be accounted for by adventitial circumstances Isolated instances

such as those of van Bogaert in which torticollis followed chronic hepatitis due to war gas poisoning or of cases of mild stationary chorea following icterus neonatorum, may well be attributed to the cerebral lesions directly related to those disorders and not necessarily consequent upon the hepatic condition Careful examination of the brain in cases of ordinary cirrhosis of the liver [68] usually fails to demonstrate any pathological change remotely resembling hepato lenticular degeneration The time factor is not responsible, for such cirrhosis also commonly follows repeated incidents of hepatitis at intervals of many years [9] Experimental evidence of generalized damage to the brain produced by causing necrosis of the bile ducts [10] or by ligature of the hepatic artery (Kirschbaum quoted by Mahaim [1]) lacks the specific histological changes of the disease under discussion

Analysis of portions of brain and liver in one chronic case has revealed a very greatly increased content of copper in the brain and liver[1] [9] but not in other cases Whether this was a coincidence remains to be investigated, but in any case the condition certainly is not copper or silver poisoning Any accumulation of these metals is regarded as a secondary effect

Rare instances of choreiform or extrapyramidal disorder associated with chronic biliary obstruction such as those reported by Pollak [11] and Schaltenbrand [1], where Alzheimer type II glial cells have been found in the cortex, striatum pallidum thalamus and dentate nucleus with degenerative cellular changes in the basal ganglia indicate that under some unusual circumstances the essential process underlying hepato lenticular degeneration can be operative in more banal types of liver disease The nature of the essential factor remains unknown although there is much to indicate some inborn metabolic dyscrasia

Treatment

The importance of glycogen in protection of the liver cell against toxic effects has been known since the time of Claude Bernard but the use of diet in the treatment of liver disorder and in facilitating regeneration of the liver cell has been greatly developed in recent years It has become clear that diets low in carbohydrate and protein and high in fat content can result in liver damage The importance of protein as well as of carbohydrate in protecting the liver cell is relatively recent knowledge Cystine and methionine in particular favor normal liver function [12] [1] Cystine in excess unless properly balanced by choline is hepatotoxic[213] The difficulty in elaborating a diet for such a disease as hepato lenticular degeneration is related to the fact that diets, which protect a normal liver against liver poisons are not necessarily adequate for essential metabolism in a damaged liver It nevertheless appears rational and logical to treat cases of hepato lenticular degeneration with a diet rich in carbohydrate and protein and low in fat content

Dimitz and Vujic [1] report some improvement in hepato lenticular degeneration with a high carbohydrate diet In our own clinic we have 3 patients who have manifested sustained improvement on a high carbohydrate (733 gm), high protein (208 gm) low fat (2 gm) diet The experimental prevention of guanidine symptoms in animals by the injection of liver extract [1] also suggests the use of extract in hepato-lenticular degeneration although no instance of its effect over a long period is on record

Splenectomy performed under the impression that Banti s disease was present has had no beneficial effect on the course of the disease

If any operative interference becomes necessary local anesthesia should be used for not uncommonly it is noted in the literature that patients have succumbed to operation and in our own experience the most careful efforts to protect hepatic function in one instance failed to achieve that object

Dystonia Musculorum Deformans

Synonyms — Torsion spasm dysbasia lordotica progressiva tortipelvis torsion dystonia

Introduction

Dystonia musculorum deformans as originally described is a progressive disease beginning most often in the first or second decade It is sometimes heredofamilial and has a predilection for children of Russian Jewish descent The disorder is characterized by muscular spasms of the flexors of the lower limbs and of certain spinal muscles particularly during attempted walking progressing to states of persistent contracture in the same muscular groups with resulting asymmetrical lordosis in the lumbar region and the appearance of similar spasms in the upper limbs and cervical spine Involuntary movements of the limbs sometimes resembling tics sometimes choreo athetoid are superimposed Dysarthria is not prominent in the early stages There are no disorders of sensation or of special sense and the reflexes are unchanged

Similar distortions of posture are seen as an after effect of epidemic encephalitis and more rarely in the course of some cases of hepato lenticular degeneration type progressive lenticular degeneration as mentioned in the preceding section and some authors (Wilson) *doubt the existence of an independent condition* The present section is concerned with the disorder as it occurs in relative purity The pathology of this variety is closely related to that of double athetosis described in the following section but there is as yet insufficient evidence to establish such pathology status marmoratus as an independent disease entity

Historical

Schwalbe [19] from Ziehen s clinic published a Berlin thesis in 1908 entitled eine eigentumliche tonische Krampform mit hysterischen Symptomen describing 3 siblings affected with the disease In the following year Ziehen presented further cases to the Psychiatric Society of Berlin He drew attention to the very characteristic torsion of the vertebral column and proposed the name tonische Torsionsneurose' In 1911 Oppenheim [1] described 4 further cases pointed out its restriction to Russian Jewish children between the ages of 8 and 14 years and proposed the names *Dysbasia lordotica progressiva* or *Dystonia musculorum deformans* Oppenheim drew attention to the ' dromedary gait ' due to very characteristic prominence of the buttocks produced by the lumbar lordosis He also noted the disappearance of the lordosis when the patient lay supine and described the varying tremors or twitches of the limbs The disorder was considered probably organic and likened to double athetosis Oppenheim described 2 further cases with choreo athetosis and thought they might represent transitional forms

Flatau and Sterling described 2 further similar but more rigid cases in 1911 and introduced the name " progressive Torsionspasmus " Fraenkel [3] suggested the term Tortipelvis Very many cases have been reported since then The reviews by Hunt [4], 1916, Jakob , 1932, Mendel [6], 1936, and Herz 1944, are recommended The present unsatisfactory state of classification of partial or unusual forms of the condition is due to the rarity of pathological studies and the absence of any known cause

Etiology

Mendel found only 5 non Jewish cases out of 40 reported by 1919 but many have been described since Non familial instances are not uncommon and only 6 families have however been reported [7] After elimination of Wilson s disease and the residua of lethargic encephalitis there remained a large group of which Herz collected 99 instances from the literature [7] In 78 per cent of these the onset was between the ages of 5 and 15, " juvenile type ", and approximately 11 per cent earlier 11 per cent later Development was normal until the onset of symptoms in about half the cases The occurrence of the familial syndrome without Jewish descent was reported briefly and unsatisfactorily by Spiller The disease appears equally common in males and females A history of exanthem or whooping cough preceding the onset is frequent and in some the disease follows an episode interpreted as an encephalitis Often however, no evidence of predisposing or precipitating cause can be found

Symptomatology

Since the earliest description of the disease the evanescent and variable early signs of the disease have caused confusion with hysteria. The appearance of the symptoms at first solely in relation to emotional disturbance or fatigue without any regular disturbance of physical signs facilitates this error. The onset is gradual and most often about the age of 11 or 12, sometimes as early as 6 years or as late as 17 years. The first symptom usually is related to one or other lower limb and appears as a transient recurrent spasm provoked by walking. In a less usual type of case to be mentioned subsequently the spasm begins in the neck. After a variable period of many months the inevitable distortion of the vertebral column appears.

Most commonly the first sign of the disease is a tendency of the child to walk on the outer margin of the foot when fatigued. The toes become flexed and the foot inverted in a spasm which may last some minutes and then relax. Gradually the knee is found to flex with each spasm, and at the same time the spasms are provoked by less exercise. Soon flexion of the hip also appears. The other lower limb or the upper limb on the same side now becomes involved, so that either the gait becomes shuffling with bilateral but asymmetrical flexion of the hips and consequent lordosis (pseudo paraplegic form, Hunt) or the limbs on one side enter into spasm at every attempt at walking (hemiplegic form, Hunt). The upper limb usually is extended and pronated. At a variable stage in this evolution of symptoms more abrupt spasmodic disturbances make their appearance. Sudden jerks of flexion of the toes with further inversion, sudden flinging protraction retraction of the extended upper limb are added to the picture, and combined with these or independently slow, almost rhythmically repeated opening and closing movements of the hand and fanning of the toes with extension of the great toes. These latter movements, identical with athetosis but in more rapid and almost rhythmic regularity, are uncommon. More usually the upper limb alternates between extension of all joints with pronation and abduction and flexion at all joints with adduction.

In the beginning both the movements and spasms are related to attempted movement and disappear in repose, but gradually there appears a persistent inversion of the foot and flexion of the wrist and fingers in the most affected limbs, disappearing only in sleep. With this persistent spasm is associated a continued contraction of the lumbosacral and psoas muscles on the most affected side producing the pathognomonic lumbar lordosis and scoliosis.

The alternative mode of onset is in the appearance of a *torticollis*, the head being drawn to one side, and some months or even years later the appearance of spasm in flexion in the opposite arm with superadded jerks or spasms of exten

sion, pronation and abduction [?, 3] The flexion inversion posture of the lower limb and "tortipelvis" are soon associated In some cases the torticollis may be the most prominent feature, the ear being literally laid on the corresponding shoulder [31, 3] Retrocollic spasm is reported in some instances [?, 3]

In such a stage the condition may become arrested and persist for many years [3], even in the familial, so called 'degenerative' type of the disease (see case 3 of Wechsler and Brock [33]) A striking variety is that presenting a mild rigidity of hemiplegic distribution, the affected limbs being from time to time subject to outbursts of wild flexion extension movements or syncinesias [16] Mild affection of one foot or one hand are described by some as "segmental fragmentary dystonia" [34] in association with postencephalitic parkinsonism but such instances as alternate fanning and plantar flexion of one foot appear to the writer to be called more properly athetosis

In about 10 per cent of cases dystonia begins between the ages of 20 and 43 (Herz) and then tends to assume a localized form usually a torticollis It should be clear from the above description that cases, such as those included as dystonia by Alexander[141] in which 'dystonic movements' have occurred from birth or the first year of life, are not considered here to belong to dystonia musculorum deformans but to congenital athetosis The difference may be one of degree, but dystonia musculorum is not generally considered a congenital disorder

The disorder in most cases continues gradually to progress the limbs of the least affected side going through the same evolution of spasms leading to increasing flexion and adduction as those of the side first affected Gradually both lower limbs enter a continued extreme flexion with adduction so that the knees become drawn into the abdomen and the heels pressed against the buttocks with great deformity of the feet (Fig 3) Both upper limbs become similarly flexed and adducted with distortion of the posture of the hand The neck muscles enter a state of spasm with drawing of the head to one or the other side and either ventrally or dorsally As the neck becomes rigid, dysarthria and facial rigidity appear The phasic movements of extension of one or both upper limbs of rotation of the neck and often of the face and eyes continue but lessen in violence and amplitude as the rigidity increases If tremor has been prominent in the early stages it also continues Speech becomes reduced to a moaning cry, and the impediments already imposed by the muscular distortion eventually negative any kind of expression so that it is impossible to estimate mentation There is no disturbance of sensation and no disorder of sphincters

Mental symptoms frequently are absent In other cases profound personality disorder of hysterical type accompanies or precedes the true dystonia Dementia is infrequent but may accompany the onset as in Spiller s family

The *course of the disease* is remarkable for occasional spontaneous remis

Fig 3 The postural deformities of dystonia musculorum deformans

sions [3] or long periods of arrest followed by the sudden development of further symptoms [4] In these respects it is further differentiated from double atheto is

Physical State

The most characteristic feature of the disorder is the assumption of abnormal postures In the beginning this change is phasic but in the nature of transitory spasm Such *spasms* are to be distinguished from ' dystonic movements such as the sudden extension of the upper limb for instance Thus, there are spasms of inversion of the foot, of flexion of the wrist and fingers, of flexion of the hip or lordosis and torticollis There are *phasic movements* of extension of the lower limb, of the upper limbs, of turning of the head, superimposed on, or in addition to, torticollis or of the face

The muscular spasms gradually become transformed into maintained postures at first provoked like the spasms only by movement or attempted movement but gradually becoming permanent and fixed by muscular shortening or contracture The postures of the foot, the hand and the lumbar spine are diagnostic in their regularity In the foot the first stage is an equinovarus a plantar flexion with inversion the toes being flexed This position, called by Hunt [4] " semilunar foot ' and by Goodhart and Kraus [18] the ' ventral foot ' because the anatomically ventral muscles are contracted later is distorted further by the appearance of spasms in the anatomically dorsal, pretibial, muscles Since the shortened tendo Achillis cannot be overcome, the tibialis anticus can have further effect only by inducing further inversion The foot now becomes completely inverted with the sole directed upwards (Fig 3) This is the ' dorso ventral foot ' of Goodhart and Kraus who demonstrated that in the early development of this stage the foot will relax to the previous " ventral " position under anesthesia Relaxation of postures under hypnosis is reported also [39] The term " striatal foot " is preferred for the complete deformity which is essentially an acquired club foot Whether or not the toes fan periodically is taken to indicate the addition of athetosis

In the upper limb powerful opposition of the thumb is an early persistent spasm with pronation of the forearm, and later flexion and pronation of the wrist and metacarpophalangeal joints bury the thumb in the grotesquely deformed hand (Fig 3)

The interphalangeal joints commonly are extended in the late stage, possibly as sole evidence of the effect of dorsiflexion The final posture is one of extreme flexion of all limbs with the unfailing lordosis (Fig 3) From the physiological point of view spasms of the extensor plantar flexor muscles of the hand and foot are primary and spasms of the flexor groups flexors of hip knee and dorsiflexors of ankle, adductors of shoulder flexors of elbow and dorsiflexion of wrist and fin

gers a secondary development which distorts the foot and hand owing to early contracture in the primary group These mechanisms will be recognized as those which in concurrent development and competition underlie the alternating posture of athetosis

Throughout the development of those maintained postures the muscular rigidity has features which differentiate it from both spasticity and parkinsonism Until contracture produces permanent shortening the posture may lapse at any moment and leave no resistence to passive movement Hence the limbs are commonly described as *hypotonic* All trace of the spasm may vanish when the patient is at rest Van Woerkom [1] notes that in such early stages the condition is closely related to intention movement A given movement is accomplished better when it is part of an habitual performance or when attention is directed elsewhere One of Davidson and Goodhart s patients[2] could throw or bounce a ball in spite of grotesque distortion of posture Each and every voluntary innervation is transformed into a stereotyped posture Co contraction of antagonists is prominent from the beginning and the essential posture is clearly the outcome of a struggle of opposing muscular groups One of our own patients had the characteristic deformity of rupture of the belly of the biceps brachii A tendency of the affected limb to move in a direction opposite to that requested for voluntary effort was called by Hunt the paradoxical phenomenon Hypertrophy of muscles sometimes occurs Both phenomena are seen also in athetosis The rigidity is intense often painful and offers increasing resistance to passive movement unlike the plasticity of parkinsonism or the clasp knife melting of spasticity It is not in any sense comparable to experimental decerebrate rigidity as maintained by some [2,4] for the reflex changes are absent and the posture in hand and foot is absent in decerebrates

The tendon jerks abdominal reflexes and plantar responses are not altered save for the difficulty in their elicitation in already active muscles At a particular stage however any stimulus tends to produce a dorsiflexion of the toes difficult to distinguish from a Babinski response

The *phasic movements* may be extremely abrupt but differ from chorea in their predictability for they follow a particular pattern in any one example They vary from case to case from waves of extension of the limbs sometimes with a slow rhythm with or without extension of the fingers or toes alternate side to side movements of the head to rapid violent sudden alternating flexion and extension of arm and leg appearing explosively with epileptoid violence One of our patients *in an arrested stage in which the violent movements were liable to appear* complained that in a crowd of people an unexpected attack would result in injury to those standing near him and his efforts to capture the wildly flinging left arm with the unaffected right hand are an unforgettable memory Such movements

closely resemble hemiballismus, but there is some regularity which distinguishes them They are best described as irregular alternations of two or more dystonic postural patterns, sometimes called ' *striate epilepsy* [37, 197]

The *torticollis* deserves special mention, for it often held to indicate an organic origin for the more common forms of isolated torticollis particularly since in some cases [?] the affection of other parts is stated not to have appeared for as long as 4 years after its onset The posture of the head is however, very violently and phasically distorted in such instances with intervals of absence of movement, in distinction from the more frequent spasmodic state with steady background seen in the isolated affection or in post encephalitic parkinsonism

The *gait* in the early stages is distinguished by the prominence of the buttocks owing to the lumbar lordosis and flexion of the hip " dromedary gait of Oppenheim Inversion of the foot may in some instances of the arrested di ea e be replaced by eversion (see case 4 of Wechsler and Brock [3]) The mental state shows no characteristic alteration, apart from personality disorder

The course of the disease is terminated only by intercurrent infection

Pathology

In general the changes in the brain appear to be very similar in all the reported cases although varying in degree of development in one or other particular Further, the histological changes appear to be widespread, even though the dystonia has been limited, for example to torticollis [41, 30] Shrinkage of the caudate nucleus and putamen is always remarked upon and may be extreme in degree (see case 1 of Davidson and Goodhart [39] It is very rare for any cavitation or softening of the basal ganglia to be seen although Nielson [4] reports a small cavity in the middle putamen in his case There is regularly a slight mottling of the upper and outer putamen in myelin stains not as intense as in double athetosis, and in parallel streaks across the substance of the putamen There is regularly great diminution of number of cells both large and small in the caudate nucleus and putamen and in some cases in the pallidum also The remaining nerve cells stain poorly and often appear pyknotic with excentric nuclei Clusters of dots of chromatin have been found in the cytoplasm by several investigators and are interpreted as nuclear debris Similar or identical changes were regularly found in the dentate nuclei of the cerebellum [39, 4] Dimitri[243] found similar changes in the red nucleus These changes are accompanied throughout by a glial proliferation which is most intense in the putamen and dentate nucleus Apart from the streaks of marbling etat marbre ' there is a general pallor of myelin sheaths in the whole lenticular nucleus most obvious in the pallidum and the ansa lenticularis is pale

These changes have been described in sporadic cases of the disease but there is no anatomical study of a case with familial history to the author s knowledge Several studies of the syndrome in non Jewish patients with a history of onset after an infection or with history of stiffness of limbs dating from early infancy have been made In these besides the changes mentioned above a striking feature has been a bilateral marbling of the dorso median nucleus of the thalamus [4] [5] [8] and widely scattered patchy cellular degeneration in the cerebral cortex

Examples of a disease characterized by epilepsy dating from infancy with idiocy or imbecility and progressive rigidity leading to flexion contractures and dysarthria have been described by Foerster as pyramidopallidal syndrome and by Hodskins and Yakovlev as neurosomatic deterioration The pathological process differs from that of dystonia musculorum in being a simple cortico pallidal degeneration and the course is more steadily progressive

The pathogenesis of etat marbre is unknown The rapid worsening with any infection throws doubt upon direct relationship to any of the specific fevers sometimes associated with the onset of the syndrome

Treatment

No treatment is known to affect the course of the condition Barbiturates lessen the tendency to spasm Hyoscine is without notable effect and is tolerated badly in some cases [2] Orthopedic correction of the deformity in mild cases is not usually attempted owing to the progressive nature of the disease and the lack of stable muscular groups for alternative use Excision of area 6 in the premotor cortex has been claimed to benefit some patients but the details upon which to form a judgment are too meagre this procedure was without effect in one case personally observed Curare has been tried by some with dramatic differential lessening of rigidity in some cases not in others It is difficult to maintain the effect Section of the upper cervical motor nerve roots has given good results in some cases when torticollis was the chief disability [4]

Double Athetosis

Synonyms — Athetose double Little s disease with involuntary movements status marmoratus congenital chorea infantile partial striatal sclerosis

Definition

Double athetosis is a symptomatic affection appearing in early infancy and associated with a variety of pathological conditions the most consistent of which

closely resemble hemiballismus, but there is some regularity which distinguishes them They are best described as irregular alternations of two or more dystonic postural patterns, sometimes called *'striate epilepsy'* [37, 197]

The *torticollis* deserves special mention, for it often held to indicate an organic origin for the more common forms of isolated torticollis particularly since in some cases [illegible] the affection of other parts is stated not to have appeared for as long as 4 years after its onset The posture of the head is however very violently and phasically distorted in such instances with intervals of absence of movement, in distinction from the more frequent spasmodic state with steady background seen in the isolated affection or in post encephalitic parkinsonism

The *gait* in the early stages is distinguished by the prominence of the buttocks owing to the lumbar lordosis and flexion of the hip, ' dromedary gait " of Oppenheim Inversion of the foot may in some instances of the arrested disease be replaced by eversion (see case 4 of Wechsler and Brock [illegible]) The mental state shows no characteristic alteration, apart from personality disorder

The course of the disease is terminated only by intercurrent infection

Pathology

In general the changes in the brain appear to be very similar in all the reported cases although varying in degree of development in one or other particular Further, the histological changes appear to be widespread, even though the dystonia has been limited, for example, to torticollis [41, 30] Shrinkage of the caudate nucleus and putamen is always remarked upon and may be extreme in degree (see case 1 of Davidson and Goodhart [39] It is very rare for any cavitation or softening of the basal ganglia to be seen although Nielson [4] reports a small cavity in the middle putamen in his case There is regularly a slight mottling of the upper and outer putamen in myelin stains, not as intense as in double athetosis and in parallel streaks across the substance of the putamen There is regularly great diminution of number of cells both large and small in the caudate nucleus and putamen and in some cases in the pallidum also The remaining nerve cells stain poorly and often appear pyknotic with excentric nuclei Clusters of dots of chromatin have been found in the cytoplasm by several investigators and are interpreted as nuclear debris Similar or identical changes were regularly found in the dentate nuclei of the cerebellum [39, 4] Dimitri [45] found similar changes in the red nucleus These changes are accompanied throughout by a glial proliferation which is most intense in the putamen and dentate nucleus Apart from the streaks of marbling ' etat marbre , there is a general pallor of myelin sheaths in the whole lenticular nucleus most obvious in the pallidum and the ansa lenticularis is pale

to such a degraded form of insanity as those demented from chorea do ' (p 138) [1] The first case described by Shaw had shown in addition to the move ments a fixed torticollis scoliosis and the lordotic gait reminescent of dystonia musculorum deformans but the abnormal posture was not progressive

Other less adequate observations were made by Allbutt (1872) and Purdon (1873) Oulmont [32] reported 2 further cases in 1878 and drew attention to the contracture or fixed spasm of muscles as in Shaw s first case and to certain more rapid or choreiform movements which appeared in attempted voluntary acts in some cases By 1892 Audry was able to collect 79 cases in the literature The onset of the athetoid movements had been observed as early as the 11th day after birth more often during the first two years Already however double athetosis had been observed to begin also in childhood 2 to 12 years and in 11 cases be tween the ages of 16 and 65 years Many of these late cases appear to have been Huntington s chorea (for example the observation of Kurella) In 9 perhaps 12 cases there had been neo natal asphyxia and difficult labor in the birth of 14 of 78 observations

In a review of the already large literature Audry concluded that double atheto sis is a symptomatic syndrome of diverse cerebral lesions Although in some cases [2] shrinkage of the basal ganglia or cavitation of the lenticular nucleus had been observed these findings were disregarded because in others no changes other than cerebral sclerosis had been found Most authors (for example Osler [4] Michaelowski Brissaud) considered the condition a variety of cerebral diple gia thought to result from prolonged labor with asphyxia or meningeal hemor rhage or from premature delivery The magnificent monograph of Sigmund Freud on die infantile Cerebrallähmung in 1897 demonstrated the fallacy of supposed birth injury or asphyxia following Dejerine he separates the double hemiplegia with greater paralysis in the arms than in the legs due to bilateral gross lesions from infantile diplegia Little s disease resulting from more subtle defect in development A brother of one of Little s original cases of diplegia supposedly caused by neonatal asphyxia had developed spastic weakness of the lower limbs at the age of 15 months and Freud collected a number of other instances from the literature of congenital diplegia in one member of a family with development of an identical affection of later onset in siblings The separation of cerebro macular (Tay Sachs) disease of encephalitis periaxialis diffusa (Schilder) of Pelizeus Merzbacher s and Hallervorden Spatz disease from the large group of diplegias has accounted for many such cases in none of which however is atheto sis a feature There still remain therefore a group of syndromes associated with double athetosis dating sometimes from birth and sometimes beginning in child hood in some associated with bilateral hemiplegia (pseudobulbar palsy) some with diplegia in others with a relatively pure athetosis

s a marbled appearance of the striatum, the "status marmoratus" of the Vogts In this most characteristic form spasmodic athetoid movements continually actuate the limbs, the face and the trunk from soon after birth onwards All forms of transition between this generalized athetosis without true spasticity and simple spastic diplegia with slight choreo athetoid movements of the extremities are encountered It is indeed likely that all transitions between double athetosis and dystonia musculorum deformans will be recorded eventually, for many of the postures and movements are shared by both The congenital onset of the former and the later onset of the latter are less strictly true than is generally supposed The condition either remains stationary from soon after birth or exhibits progression in two or more episodes

Historical

This subject from its earliest history has been plagued by confusion of terminology Continued distortion of the limbs without affection of the mind has been recognized under various names since the middle ages when, according to Parkinson[74], who quotes Linnaeus, it was known as *hieranosos* or the "morbus sacer" He cites the report of a case by Macbride in 1772 The early recognition of involuntary movements in limbs subject to hemiplegic paralysis and their varied and uncertain appellation as post hemiplegic chorea (Weir Mitchell), athetosis (Hammond), mobile spasm (Gowers), choreoid movements (Gowers), has been described in the introduction to this chapter In the classical description of cerebral diplegia Little [0] recognized that affection of the upper limbs, when it occurred, resulted in a spastic posture of pronation with semi flexed wrists the fingers incapable of perfect voluntary direction "In a few cases a distinct resemblance to severe chorea is perceptible" (p 303) Little also notes extreme sensibility to touch, the whole condition reminding the observer of tetanus" Such is the condition generally called diplegia with athetosis The first adequate description of what is now called *double athetosis* was given by Shaw [51] in 1873 under the title "On Athetosis on Imbecility with Ataxia" The "ataxia" referred to the difficulty in walking The condition was congenital "or at any rate supervening soon after birth" The movements of the hands and feet were identified with the "athetosis of Hammond, but in addition there were movements of the muscles of the head neck and face He gave a brilliant description of the movements with illustrations There was no history of chorea in the families The condition had been stationary since birth In spite of his inclusion of the word "imbecility in the title he stated "though there is a congenital feebleness of intellect, this feebleness does not increase on the contrary, when educated, the subjects of it show considerable intelligence, and never descend

claims that disease of the pallidum is the important feature of double athetosis, and a few cases of progressive rigidity with athetosis, with loss of myelin in the pallidum, etat dysmyelinique, Vogt[51] have been described

Nevertheless there remains the fact that the usual lesion in non progressive double athetosis dating from birth or within the first year appearing gradually without preliminary double hemiplegia usually has status marmoratus of the striatum The affection sometimes is hereditary more often familial [64] but usually isolated

Symptomatology

Since the movements of the young child in the first months have as Freud [49] remarks many features in common with athetosis and chorea and the postures assumed by the limbs present something of the flexor rigidity associated with diplegia it is often difficult to discern the first onset of the true disorder In a small proportion of cases the scene opens with a convulsion following which spas modic rapid jerky movements are first noticed in some the whole progress of development appears to be natural until the age of 2 or 3 years when usually after a convulsion and often with a febrile illness the involuntary movements appear Most usually the abnormal movements of the limbs are noticed within the first 6 months for they then become sufficiently violent to cause difficulty in bathing nursing etc An abnormal sensitivity to noise usually is noticed about the same time so that the child screams and has spasms whenever approached The movements are chiefly in the upper limb and vary considerably from patient to patient being in some the deliberate opening and closing of fingers extension abduction and flexion adduction of the upper limb resembling but a little more rapid than post hemiplegic athetosis There may be superimposed sudden jerks of extension of movement of the head and of grimacing Depending on the degree of spastic diplegia present spastic extension of the lower limbs with scissor ad duction will have appeared before the on et of the involuntary movements

The degree of mental retardation varies greatly In severely affected cases there is no acquisition of control over the sphincters only a few sounds may repre sent speech and little sign of intellectual function save perhaps recognition of parents and indication of pleasure or displeasure may develop This degree of mental disorder is unusual More often the patient appears moderately intelli gent but lacks application so that he remains childish and simple Some learn to read but this is exceptional Pathological laughing and crying are frequent In a simple diplegia with athetosis of the hands the intellectual capacity may be unimpaired

The movements reach full development at about the end of the first year and then remain stationary Some difficulty in articulation and swallowing are the

The common striatal lesion of double athetosis was described clearly by Anton of Graz in 1896 The excellent clinical description is followed by a detailed pathological report which mentions the myelinated fibers in the scars in the hinder halves of the lenticular nuclei The movements are called "chorea but the terminology is not in fact important, as the following description will show In 1911 Oppenheim and Vogt [60] published the pathological findings in a case of hereditary athetosis affecting upper and lower limbs and associated with dysarthria and dysphagia There was only very slight reflex change and no true paralysis A generalized microcephaly was found, but in addition a great shrinkage of the striatum together with a peculiar scar in the upper putamen and head of caudate nucleus which from its resemblance to the streaks on marble was called '*etat marbre* ' or *status marmoratus* In subsequent papers [61 6] it was maintained that the status marmoratus was the direct exciting cause of bilateral spasms accompanied by athetoid movement, rhythmical oscillations of the head, associated movements, pathological laughing and crying as a congenital non progressive anomaly with the absence or almost complete absense, of paralytic phenomena The disorder was called a 'pure striatal syndrome", and it was maintained further that the dysarthria was the result of an affection of a supposed speech function of the lenticular nucleus

In later papers the Vogts [63 51 64] discuss further cases of the striatal syndrome They now found 'spastic phenomena, meaning spasms of varying duration, in the more severe cases affecting the lower limbs more than the upper as in Little s disease often with extensor type of plantar response but not a true Babinski Control of sphincters was retained and intellectual function often but slightly if at all altered In the slighter degrees of the same affection there was generalization of hyperkinesis , which includes choreic movements resembling athetosis Pathological laughing and crying were found frequently Emotional stimuli or effort increased the hyperkinesis Severe disorder of articulation, mastication and deglutition were the rule

The syndrome of status marmoratus thus developed by the Vogts, has been criticized from many points of view Bielschowsky [65], Lowenberg and Malamud [60] and others have found widespread status marmoratus in the cerebral cortex in cases of infantile cerebral paralysis with athetosis epilepsy and mental enfeeblement, thus destroying the conception of a striatal syndrome' Onari [6] and others have maintained that a variety of etiologies developmental or acquired even lead to status marmoratus and Scholz [69] and Lowenberg and Malamud [66] claim evidence of an attack of encephalitis at the onset of their cases The border line, if any between Little s disease and double athetosis has no pathological definition Hypermyelination of glial scars the characteristic feature of status marmoratus occurs to a slight degree in other conditions [6] Lastly Jakob [?]

the identity of the two syndromes The eye muscles alone appear unaffected except to be deviated strongly to one or other side in a sudden jerk of head and eyes together If intellectual function permits perfect control of the sphincters is gained and maintained a powerful argument against those who claim the disorder results from loss of cerebral inhibition

The movements are intensified by excitement or noise but continue in a totally irregular fashion at complete rest They disappear completely or almost completely in sleep some movements of the fingers sometimes remaining From time to time a jerky movement at one or other joint is added to the other movements and this may be a sudden extension of a finger of an elbow of the neck or flexion, then extension of a whole limb They are prominent when the patient attempts some other movements hence their name of associated movements (Mitbewegungen) as described first by Anton These rapid movements are those called chorea or choreo athetosis depending on the degree to which they dominate the general picture As Collier has remarked the title of congenital chorea to designate cases when these rapid jerky movements are prominent is unfortunate for the condition is neither truly congenital nor are the movements comparable to chorea except in speed The jerky movements are localized and affect the proximal parts of the limbs most and like myoclonus of which they are a variety they affect the tongue and palate in some instances

In some patients the athetoid movement is seen only in repose usually then only in the hands face and neck The upper limbs then are spastic in a posture of strong adduction flexion of the elbows wrists and metacarpophalangeal joints and extended fingers The lower limbs are extended and adducted with talipes equinovarus the toes being extended and periodically fanned Any sudden or unusual activity then provokes spasms a powerful extension of both upper limbs the posture of the hands remaining unchanged and the lower limbs show added adductor spasm Dorsiflexion of the spine with retraction of the head and added spasm of the face accompanies such attacks The resemblance of such a patient to the condition described in the preceding section as dystonia musculorum deformans is striking although the slight amount of contracture and the stationary nature of the disability form distinguishing features

The tendon reflexes usually are slightly exaggerated and the plantar response most often is extensor with fanning of the toes It is difficult however to be sure that the stimulus has not excited an athetoid movement and the response may vary with the phase of movement Vogt has discussed the meaning of this extensor response finding no damage to the pyramidal tract in cases that had exhibited it

No sensory changes or disorders of the special senses have been reported Epilepsy and tonic attacks of uncertain nature are frequent in those with severe

rule The acquisition of natural posture is greatly delayed so that inability to hold the head up usually is an early sign Ability to walk, if acquired at all, is very delayed

Physical Signs

The most striking feature is the involuntary movements which continually activate the face neck and upper limbs and to a less degree the lower limbs The original description of Shaw [1] is characteristic of the most usual variety 'They consist of a slow protrusion of the head forwards and upwards to one side or the other, and of its retraction downwards and to the other side ' "The facial movements are very extraordinary, and give rise to varying expressions, the most frequent being that of a broad grin, owing to spasms of the retractors of the angles of the mouth To this succeeds — or may succeed — a comparatively blank look from relaxation of those muscles but the marks of the wave are shown in the furrows left The occipito frontalis may contract, elevating the eyebrows and giving the expression of wonder, which expression may directly afterwards pass into that of a broad grin ' ' Like the face muscles, those of the fingers seem independent one of the other, for not only do they bend and extend themselves capriciously, out of unison with the others, but flexions happen now at the second then at the proximal joint while the fore arm is ever on the move from pronation to supination and back again " "The upper arms are not affected to the same degree as the fore arms and hands, and only in some are the lower extremities affected in the particular manner Two distinct kinds of alteration may be discovered in the one the gait resembles the tabic ' form often seen in 'general paralytics and in these persons muscular movements of the toes resembling those of the fingers may be seen in the other class the defect seems to be a want of co ordinating power combined with a distortion of the pelvis owing to spinal curvature which is more or less pronounced in all the cases and consists generally of a primary curve in the dorsal region and secondary curves in the cervical and lumbar ' (p 133–4) Shaw [51] and Michailowski [5] provide good illustrations

Close examination of the muscles reveals a constant antagonism of contraction and indeed the strange postures result from this asynergia The tightly stretched cords of the platysma muscle opposing the slow dorsiflexion of the head opposing action of the mandible and facial muscles one opening the mouth while the other closes it are striking examples It can often be observed, especially in the lower limbs that when the patient attempts to perform one simple movement the antagonist contracts as first described by Anton [9] This process is identical with the paradoxical phenomenon of Hunt in dystonia and is further evidence of

eralized affection of the cerebral cortex The cerebral cortex then presents the *appearance of microgyria on its outer surface The athetosis mobile spasm or* rapid myoclonic movements are always more marked on the side opposite to the most developed striated status marmoratus

The nature of the scarring is unique both because of the appearance of a meshwork enclosing mildly affected nerve cells and because of its continuity and finally its *hypermyelination* The scar is visible most clearly in the sections *stained with myelin stains owing to its containing a meshwork of finely myelinated* fibers Silver stains show that there are corresponding axis cylinders Such an appearance might be supposed to arise from the shrinkage of the nuclei were it not for the fact that the hypermyelinated scars arise where there are normally no such fibers e g in caudate nucleus cortex Alexander[1] [1] was unable to stain glia in the scar in his cases and considers the fibers to be an aberrant tract In view *of the lack of continuity with any supposed tract the well defined glia demon strated* by Sholtz Bielschowsky and others and a dense fibrous stain of the scar both with Mallory s phophotungstic hematoxylin and Victoria blue in our own case we conclude with Bielschowsky that the condition is one of abnormal gliosis with a special tendency to deposit myelin Since deposition of myelin is a *function of glia the primary disorder is considered by us to be a specific variety of gliosis*

It has been noted by Norman [7] that when the marbling is widespread the degree of gliosis varies from one area to another and is absent in some streaks of hypermyelination In the patient of Case the gliosis and hypermyelinization were unrelated Further hypermyelination has been found without marbling and *in small degree in the scars of traumatic lesions in general paresis in von* Rechlinghausen s disease in telangiectasis of the cortex [64] and in carbon monoxide poisoning We regard these minor degrees of the phenomenon as further evidence that the condition depends on alteration of glial function an alter ation which in some part of its evolution or involution may not be associated *with scarring but which nevertheless is understood best as primarily a glial dis order*

It will be recalled that double athetosis is classified as a variety of cerebral diplegia Before the recognition of status marmoratus the true Little s disease (excluding double hemiplegias from bilateral acquired gross lesions and progres sive syndromes such as amaurotic idiocy and Schilder s disease) was known to be associated *with acquired cortical sclerosis often microgyric* The pathologi cal entity called status marmoratus and approved as such by Bielschowsky [6] has now been shown to be the basis of a common type of this microgyric cortical sclerosis and by its affection of the striatum of the double athetosis occurring alone or in association with the microgyria The contention of the Vogts that

mental affliction and both are related to extension of the pathology to the cerebral cortex

Patients exhibiting a spastic diplegia with spastic extension and adduction of both lower limbs with mild choreo athetoid movements of the hands but lacking the movements of the head and face are a more usual variety of spastic diplegia, the relationship of which to the generalized syndrome described above is uncertain (see Pathology) Severe bilateral cerebral disease in children causing bilateral hemiplegia can also result in dysarthria and dysphagia with the development of athetosis in the hands Here however, the abrupt initial onset, whether from birth trauma or inflammatory process is more clearly defined and the spastic disorder is a remainder of a greater degree of initial paralysis Pathological laughing and crying may occur also The increased lip sucking and chewing reflexes and the loss of previously controlled sphincters are points of differentiation

Reported cases of later onset, including many reported in the earlier literature (compare Audry) probably are either varieties of dystonia musculorum deformans or of Wilson s disease, as already described

Pathology

Since the description of the peculiar marbled scarring in the putamen and caudate nucleus by C Vogt [60] [61] this condition has been the most consistent finding in double athetosis The condition was clearly described originally by Anton [9] in a patient in whom involuntary movements appeared after severe scarlet fever at the age of 9 months and then often persisted until death at the age of 9 years A cicatrix occupied the caudal four sevenths of each putamen It was noted that myelinated nerve fibers were involved in the scar The Vogts[51] have described 8 cases, in which scarring of the putamen and caudate nucleus occurred of varying degree and extent but with the characteristic marbled appearance in myelin preparations The correlation of affection of different segments of the body with oral, middle and caudal portions of the structure claimed by the Vogts is not convincing to this writer for it would seem that the most lateral border of the putamen is always most affected, and that pure athetosis can appear with lesions of the posterior or caudal half as in Anton s case or rostral portion as in Vogt's second case Steinberg

The preponderance of continued spasm whether paraplegic or torticollic appears most often with affection of the rostral half of the putamen and caudate nucleus The presence of patchy scarring of the cerebral cortex in cases with associated epilepsy and dementia is shown in the cases of Bielschowsky [6], Lowenberg and Malamud [66] and Meyer and Cook [46] In case 3 of Lowenberg and Malamud the striatum was only slightly affected compared with severe and gen

Treatment

No treatment is known to influence the essential pathology of the disease Nor has the use of physical therapy such as heat massage or electricity in various forms proved of benefit The value of exercises orthopedic treatment and surgical interference with nervous pathways obviously has to be assessed in relation to the severity and localization of movements and the degree of mental affection Phelps [4, 15] who has great experience in such special training indicates that the first step is to obtain simple voluntary movement in a state of relaxation Ability for sustained application and concentration is an essential for the success of such treatment [6]

Tendon transplantation arthrodesis and splinting which might conceivably have a very doubtful place in the treatment of a unilateral spastic athetosis are impossible in the generalized condition The involuntary movement is not stopped by paralyzing one muscle for the balance is upset in others which then show the movement Section of posterior nerve roots and cross anastomosis of motor nerves have been abandoned Resection of motor or premotor cortex has been used successfully in a number of cases since first reported by Horsley in 1909 The operation has been modified by Bucy [8] who resects area 6 in the premotor cortex and favorable results are reported[2] Failures with the Horsley method have been reported also[5] and a small personal experience has been disappointing Putnam[1, 4] has advocated cordotomy of the extrapyramidal tracts in the cervical region and reports encouraging results Athetosis limited to one upper limb naturally is more favorable for either operation and in bilateral cases the most that can be expected is greater facility for one of the hands in a few simple manoeuvers

Of the sedative drugs the barbiturates appear to have the greatest effect and Bucy [3] reports suppression of movements for 2 days following single anesthetic dosage Burman [4] and Putnam have used curare with some resultant lessening of movement but the drug has not been found satisfactory for continued use owing to the large doses required to maintain a worthwhile degree of suppression It can be concluded therefore that there is at present no satsisfactory treatment for double athetosis

PROGRESSIVE RIGIDITY WITH ATHETOSIS

Under the above heading may be grouped an assortment of rare syndromes exclusive of hepato lenticular degeneration where tremor usually dominates the picture and of dystonia musculorum deformans Whereas the course of the latter disease is episodic the following syndromes share a steadily progressive course

status marmoratus is a syndrome of the corpus striatum has been gradually criticized on the ground that other structures than the basal ganglia may be involved that the condition is not congenital and not necessarily associated with athetosis [8] [173] In defense of the Vogts it should be said that they considered the condition a defect in germ plasm', which its sometimes hereditary and familial course surely indicates, and confirmed the findings of Anton that the striate lesion is responsible for the athetosis

Norman [1] has published an account of the brain of an epileptic idiot with widespread ulegyria and some microgyria of the cerebral cortex together with bilateral status marmoratus of the dorsal portion of the putamen No athetoid movements had been observed in life, but the clinical details are meagre The author concluded that the involvement of the cortex accounted for the absence of athetosis We would, however, consider the case a valuable link between generalized mycrogyria (fetal malformation with heterotopic collections of nerve cells) ulegyria (acquired distortion of the gyral pattern) and status marmoratus of the putamen

We have indicated already that a similar condition with different distribution is the basis of dystonia musculorum deformans then involving the thalamus as well as the striatum and cortex Although dystonia musculorum deformans is considered a progressive disease of much later onset than Little s disease there are cases of early onset of long remissions and a curiously frequent history of some rigid condition antedating the dystonia and persisting since infancy Further, double athetosis frequently (in one sixth of all cases [3]) exhibits the postural changes of dystonia in mild degree and very often presents the " dystonic movements in the form of myoclonus or ' chorea '

We, therefore, submit that the condition ' *status marmoratus* is not only an independent pathological process, affecting the brain to a varying extent and depending on a specific disorder of neuroglia, but that its common clinical manifestations are either Little s disease or double athetosis or a combination of the two when the onset is in the first two years of life, and dystonia musculorum deformans, when the onset is later Any of the conditions may be associated with epilepsy and dementia Thus we would widen the disease category to include other than striatal disease without prejudice to the remarkable predilecti n of the process for the striatum established by the Vogts In each case the process is liable to exacerbation following infective illnesses owing to a specific sensitivity of status marmoratus in this respect The pathogenesis of the condition remains in doubt Its relationship to asphyxia neonatorum as maintained by the Vogts, is as untenable as the supposed caudal relationship of asphyxia to Little s disease [9] [0] The cause is as unknown as is that of the characteristic gliosis of hepato lenticular degeneration

reported also in other families The characteristic lesion is a deep brown pigmentation of the globus pallidus and pale portion of the substantia nigra without softening In sections the pigment is seen to occupy some of the large ganglion cells some of it to lie free in granules of varying size in the tissue spaces some to be collected in the perivascular space There is a great increase of fibrous glia The pigment was found to be composed of iron salts

The vascular calcification noted in the vessels of the basal ganglia in advancing age by Aschoff and others was shown to be composed of iron salts by Hurst and is found in 50 per cent of brains of persons without extrapyramidal disease It is situated chiefly in the walls of vessels of moderate size but also lies free in the tissue in small granules and becomes evident after the age of 20 years Hadfield[6] considers this siderosis to be the expression of a slow involutional atrophy affecting the globus pallidus in at last 60 per cent of people over the age of 30 years He considers the siderosis of Hallervorden Spatz disease to be a very early manifestation of the same process The pigmentation and gliosis of the disease is however much more intense than is ever seen in the senile brain [6]

Helfand described an isolated case in a woman with onset at the age of 11 and death at the age of 25 There was progressive generalized rigidity without athetosis but with intention tremor in one limb Besides the characteristic pigmentary scarring of the globus pallidus ballooned cells were found in the sixth cortical layer throughout the brain together with a mild gliosis The resemblance of this ballooning to that of Niemann Pick s disease suggested interrelationship which was however not supported by any description of visceral lesions A further variant is that reported by Osman and Schukru wherein the cerebral cortex was widely degenerate and lesions closely resembling those of the Hallervorden Spatz syndrome occupied the inner portion of the pallidum The substantia nigra and putamen were affected in less degree Progressive rigidity with athetosis and dystonia had resulted

Other Conditions

The extraordinary condition reported by Woods and Pendleton in 14 Chinese in families in a famine area evidenced clinically by the sudden onset of torsion spasm and rigidities improving in some and progressive in others appears to bear some relation to the Hallervorden Spatz disease In the only autopsy available there was yellow necrosis of the caudal two thirds of the globus pallidus on both sides and of one substantia nigra Granules of pigment were not observed There was a moderate degree of meningeal inflammation This may be called *Woods Pendleton disease*

Status Dysmyelinatus

Under this title the Vogts[31] described a condition of shrinkage of the pallidum with striking pallor of the ganglion in Weigert sections Two cases are described One was a premature child who began to have convulsions at the age of 6 months with the development of a general rigidity with athetosis which ultimately involved the face and was associated with dysarthria Intelligence was limited Increasing spasticity of the lower limbs resulted in severe contracture in flexion Death occurred at the age of 10 In the second patient the spasticity and movements were noticed in the first month and progressed until death at the age of 13 There was great shrinkage of the pallidum, especially the outer segment the corpus Luysii and to a less extent the thalmus There was a notable loss of striopallidal and striopetal pallido thalamic and pallido subthalamic medullated fibers The substantia nigra and red nucleus were unaffected In one case the caudate and putamen were a little shrunken in the other unaffected The loss of striopetal fibers appeared disproportionate to the degeneration in the striatum Jakob[93] and Ammosow [9] described further instances and regard the condition as non specific, occurring as a variety of Little s disease and also resulting from encephalitis The cause is however, unknown and its relationship to Little s disease uncertain There is a very close resemblance to the cases described as ' juvenile paralysis agitans ' or progressive atrophy of the globus pallidus (see description in previous section) where tremor accompanied progressive rigidity

The Syndrome of Hallervorden and Spatz

Fischer [81] and Rothmann [1] described a condition in children, who were normal at birth with slowness in walking and talking who graduallv developed spasticity of the extremities with choreo athetoid movements and dysarthria about the age of 5 or 6 On section of the brain a striking brownish discoloration of the pallidum was noted In Weigert preparations there were numerous sclerotic patches in the globus pallidus, the putamen and caudate nuclei remaining intact These cases were cited by the Vogts as examples of ' status dysmyelinatus ', but the mention of brownish discoloration in both and a destructive sclerotic pallidal lesion with chalk like ' deposits in it [83] identifies the disorder with that described by Hallervorden and Spatz [84] in 1922 in 5 sisters of a family of 12 The father and mother were in normal health The affected children had commenced to suffer from increasing rigidity without reflex changes and progressive mental deterioration at the age of 7 to 9 years As the disease progressed there were contractures, and in one the eldest athetoid movements of the hands and face appeared Death occurred between the ages of 16 and 27 Athetosis has been

Huntington's Chorea

Synonyms — Hereditary chorea chronic progressive chorea adult chorea

Definition — Huntington's chorea is a progressive degenerative cerebral disease with onset usually in middle life inherited as a Mendelian dominant. It is characterized by the appearance of involuntary movements in the limbs and face and ultimately of the whole body in association with a slowly progressive simple dementia.

Historical

The word chorea has a long history and at one time or other has been used to cover all types of involuntary movement. In the Middle Ages outbreaks of convulsive and ecstatic manifestations affecting whole communities are described as Saint John's Saint Guy's or Saint Vitus' dance according to the locality and the saintly shrine whose healing virtues were esteemed [35]. After the description of rheumatic chorea *chorea minor* or *chorea anglorum* also popularly called *Saint Vitus dance* the epidemic variety was called *chorea magna* or *chorea germanorum*. An outbreak of such choreomania occurred as recently as 1867 (Davidson [98]) in Madagascar among superstitious people who were excited by social and political changes.

The disorder termed *chorea electrica* by Dubini appears to have been myoclonic twitchings similar to that associated with epidemic encephalitis and not resembling true chorea. The *electric chorea of Bergeron and Henoch* probably was myoclonic epilepsy.

Hereditary chronic chorea of adults was known to many observers in the early nineteenth century. Be nt (1810) and others having reported cases. A brief account of the disease is given in Dunglison's Practice of Medicine (1841) in the form of a letter from a Dr Waters [b] who had observed cases in New York State where it was known as the "magrums". It is known [90] that Gorman of Luzanne Pa wrote a thesis on the subject in 1848 but the account has been lost. See [70] in a comprehensive review of chorea in general in 1850 recognized hereditary chorea but did not clearly differentiate it. Lyon while a house physician at Bellevue Hospital published a paper on "Chronic Hereditary Chorea" [30] in 1863. His cases were seen near Greenwich Conn near those to which Waters referred and he records some small family histories.

The classical account is that given in 1872 by George Huntington whose cases had been observed in and near Easthampton Long Island by himself and his father. He discusses the hereditary nature of the disease the tendency to insanity and suicide in the sufferers and the ages of onset of the symptoms. The cases were in families that had been among the earliest to settle on Long Island.

It is fitting to remark here that a very closely progressive rigidity with choreo athetosis is a feature of the *Pelizaeus Merbacher disease* In this case, however nystagmus, incoordination and ataxia are prominent as well as marked generalized spasticity with appropriate reflex changes A spreading demyelination in the white matter of the brain affects the basal ganglia secondarily An interesting clinical report of the disease in 2 cases with summary of the literature is given by Scheftel [91]

Damage to the basal ganglia accompanied by yellow pigmentation is commonly found after death from *icterus gravis neonatorum* (Kernicterus) If the child survives rigidity of the limbs, often with choreo athetosis commonly occurs in association with *feeblemindedness, convulsive disorder*, blindness and other evidence of widespread additional cortical injury Loss of ganglion cells in the lenticular nucleus both putamen and globus pallidus, and often of subthalamic nuclei in addition are found [9, 93] The possibility that milder degrees of this disorder lead to the Hallervorden Spatz syndrome has been raised [93], but in our own experience and that of others [94] a mild choreo athetosis persisting into adolescence without progression of signs or symptoms is the usual result

The *spastic pseudosclerosis of Jakob and Creutzfeld* or the *Jakob Creutzfeld syndrome* might also be considered as a possible variant of the group of cases showing progressive rigidity with choreo athetoid movement These movements are, however, a rare feature, the disorder is referred to more fully on a subsequent page under the general heading Other Forms of Adult Chorea

General Features of the Disease

Huntington's chorea is an uncommon disease although the presence of one or two families in one locality may give a different impression Hughes[4] gives a map showing its patchy distribution in Michigan She found the diagnosis made in 1 1 1 6 and 2 4 per 1 000 first admissions to three mental hospitals Critchley[3, 8] found 74 cases among 119 787 mental hospital patients (0 6 per thousand) in England Many cases however are never admitted to such hospitals

The *age of onset* may be at any time from infancy to old age In 460 cases Bell[11] found a mean age of onset of 35 5 years There were 9 cases of onset under the age of 10 years and 15 over 60 By far the greater number of patients first show signs of the disease mental or choreic between the ages of 30 and 50 The mean age of onset in Davenport and Muncie's series was 37 8 years Hughes 37 1 years Minski and Guttmann 42 4 years

The age of onset in symptoms tends to similarity in any one family but this is by no means constant From Bell's tables it is seen that parents who developed the disease under 35 years of age all begot children in whom the onset of the disease occurred at less than 35 years of age whereas only 6 of 32 choreic children of parents who developed chorea after their 50th year developed symptoms as late as this Davenport and Muncie[3] found no evidence of anticipation of age of onset in subsequent generations if the fallacy of false selection of progenitors of late onset is excluded

The *incidence* of the disease in the family varies greatly In some families nearly every living member is affected in others perhaps only one in each of two or three large generations The percentage of children of one affected parent in Bell's series is 55 with negligible difference in transmission by males and females

The *duration* of the disease to time of death obviously is affected by many factors besides the rate of progress of the disease itself very variable The mean duration in Bell's series was 13 7 years

Huntington[3] says When either or both parents have shown manifestations of the disease one or more of the offspring almost invariably suffer from the disease if they live to adult age but if by chance these children go through life without it the thread is broken and the grandchildren or great grandchildren of the original shakers may rest assured that they are free from the disease Unstable and whimsical as the disease may be in other respects in this it is firm it never skips a generation to manifest itself in another These statements are in general true as of any dominant inheritance but there are 6 families on record where both parents of two subsequently choreic generations were known to be free from the disease to an advanced age The first family recorded by

and one of the New Jersey families described by Gorman was definitely traced to the Easthampton group

Huntington s contribution was abstracted in Virchow Hirsch s Jahrbuch for 1872 and received immediate appreciation in Europe where in a growing interest in hereditary an affection which manifested itself so late in life was hitherto unrecognized Reports of affected European families soon appeared It was observed in negroes[3, 304] and in other races in all parts of the world

The difficult task of tracing the ancestry of the original American families was pursued by Jelliffe[301] and Tilney[30] and brought to a conclusion by Vessie[3] who traced them all to two brothers and their families who sailed from Bures to Suffolk England, in 1630 to arrive in Boston Bay From them in direct descent over a period of 300 years approximately 1 000 cases were known in 1932 The early history traced in the early records of colonial courts of trials for witchcraft and misconduct is a pathetic legend of persecution[0] There appears to be no doubt that similar persecution had preceded the emigration and a pedigree chart by Hattie indicates a similar "pilgrimage of misfortune" of Huguenots in another group from France to England and thence to Halifax Vessie gives an account of the evidence of witchcraft given at the trials and of the popular belief of the times that the involuntary movements represented a derisive pantomime of the sufferings of the Saviour during crucifixion also mentioned by Lyon[300] There were no relatives of the original families remaining in Bures in 1934[308] although Huntington s chorea was then more common in Essex and Suffolk than in other parts of England and Wales The migrations of the original Bures descendants to various regions of the United States were traced by Davenport and Muncie[3, 9] Hamilton[310] traced cases in Iowa not only from the Long Island families but also directly from Germany Ireland, Norway and other European countries

A large literature has accumulated on the subject, over 400 references being collected in the Huntington number of Neurographs in 1908 and many since The disease has been studied extensively in Europe and the monographs of Huet[311] Entres[31] and Josephy[312] are notable Although inheritance of the disease by a dominant gene had long been indicated statistical confirmation has appeared only recently (Sjogren[14]) A valuable correlation of pedigrees from the literature has been made by Bell[315] Many more have been charted since e g Minski and Guttmann[3 5]

The pathology of the brain had been described by Sinkler[116] Osler[31 318] and others but the changes in the basal ganglia had been overlooked until the work of Jelgersma[78] in 1909 Alzheimer[3 9] Pfeiffer[3 0], Marie and L Hermitte[1], the Vogts[1], Dunlap[3] and others Anglade[3 3] in 1909 first attributed the movements to the striatal disease

Symptomatology

Somatic Symptoms — The most striking and characteristic feature of the disease is the muscular movements from which the name is derived Osler[3 7] noted that they are slower, less brusque or jerky than those of Sydenham's chorea and sometimes influenced by the will He likens them to Friedreich's ataxia Waters [9] in the original description says although the descriptions of chorea in the books apply very well to this disease it nevertheless seems to differ in several respects from ordinary chorea First it rarely occurs before adult age Second it never ceases spontaneously Third when fully developed it wants the paroxysmal character This last remark which implies a *continuity of movement* is the most notable difference The movements are not a succession of abrupt contractions in single muscles or one or other group of muscles but series of graduated contractions which so to speak flow from one muscle group to another The resulting movements have a smooth waxing and waning which have a wave like fluctuation in contrast to the abrupt jerks or lapses of movement characteristic of Sydenham's chorea

In their mildest degree they are difficult to distinguish from simple restlessness or fidgets The patient does not keep still the head is moved this way or that the leg shifts position the facial expression is disturbed by a grimace The movements in this slight degree are purposive and if watched carefully are seen to repeat in certain patterns which are peculiar to each patient For this reason they are often confused with tics from which they differ in that the pattern is less stereotyped i e confined to the generality of the movement and not to the detail has more symmetry and is less abrupt Thus a flexion of the neck with a slight turning of the head to one or other side and return to normal posture will take from 4 to 5 seconds and will be repeated at irregular intervals more or less frequently accordingly to the state of excitement of the patient and the state of the disease In the head nodders this for a long time may be only abnormal movement In the hand an extension of all the fingers followed by a flexion is a common and characteristic movement accomplished in about 2 seconds This play of movement of all the fingers is particularly evident as the patient walks In the face pouting of the lips is a common pattern usually accompanied by their separation on one or other side and partial or complete protrusion of the tongue The tongue sooner or later is rolled to one or other side when the mouth is open All these movements are purposeless and are related to voluntary movement only in that they are superimposed upon it

As the disease progresses movements of the lower limbs and of the proximal joints of the upper limbs appear Movements of the trunk usually are slight until late stages The variable and unpredictable movements are added in great variety

Osler[317] is a well documented example of unaffected parents of a severely affected family reaching the age of 87 and 85 respectively, and in a similar family recorded by Smith[3 6] the parents reached the ages of 93 and 87 without symptoms Bell notes other similar cases

Davenport and Muncie[00] noted *distinct family types*, biotypes peculiar in the age of onset rapidity of progression, prominence of movements of the hands face or head "head nodders", and extent of mental deterioration Unsteadiness of gait is also a peculiarity of manifestation in some families Monozygotic twins develop the chorea at the same age and in one pair it was complicated by behavior difficulty in both at the same period[7 7]

The question of the existence of mental deterioration without chorea as a variety of the disease is disputed Bell concludes and the pedigrees certainly suggest that feeblemindedness in choreic families is probably a separately determined and independent hereditary factor There are numerous cases on record, where the choreic movements occurred only very late in life, after a long history of mental change

The cases cited by Davenport and Muncie as examples of dementia without chorea are described too briefly to avoid the objection that the mental state, delusional insanity, mania, etc was a coincidence or alternatively would have been associated with movements had the patient survived long enough The family reported by Curran[3 8] is fully documented and supports Davenport's conclusion, except that an unsteady gait with dysarthria was inherited in place of the usual "movements"

On the other hand there are a number of cases on record[309] where *progression was limited*, so that the movements remained stationary at either slight or severe stage and remained independent of the dementia which either failed to occur or progressed independently Senile tremor without choreic movements also has been described in otherwise unaffected members of a number of choreic families and in the same families parkinsonian rigidity is reported occasionally The relationship of this type of tremor and rigidity to the essential disease process is uncertain

Epilepsy has been reported in a number of instances and some authors are inclined to include this as a manifestation of the disease We agree with Minski and Guttmann that the general evidence indicates that this with feeblemindedness is not closely linked with Huntington s chorea and shows evidence of being a separately inherited trait

Huntington's chorea has no particular relationship to Sydenham's chorea Hughes[3 4] found 17 instances of Sydenham s chorea among unaffected Huntington stock and 3 instances of previous Sydenham s chorea in those who later developed the hereditary type

power of contraction is not impaired the tendon jerks and other reflexes not altered *There is no disorder of sensation or of the control of the sphincters*

The movements are lessened during febrile illnesses [1] but reappear immediately afterwards They are increased in pregnancy and their first appearance not infrequently is in the course of a pregnancy In an individual subsequently affected by the disease movements have been reported to accompany the toxemia of a pregnancy only to disappear thereafter until their progressive onset years later The first onset also is precipitated commonly by a fright or by trauma

Mental Symptoms — In common with the other organic dementias Huntington s chorea is notable for a *progressive defect in memory* particularly recent memory and recall The patient complains of difficulty in concentration of forgetfulness of feeling stupid or dull There is usually awareness of or insight into the difficulty in recall function and some regard this as specific These features are however shared by arteriosclerotic dementia and some cases of presenile dementia e g Pick s disease For the same reason there is nothing to support the assumption of Kleist' that the disturbance in motility is in any way connected with the disorder of thinking The loss of memory ultimately is associated with loss of apprehension judgment and insight so that the patient becomes careless in habit dirty and incontinent in advanced stages of the disease The course is, however, so variable that whereas in one member of a family a state of profound dementia is reached in 5 years in others the disturbance is compared to a mild memory defect for as long as 20 years or rarely may have no clearly demonstrable defect at any time

Accompanying the dementia and usually preceding it by one or two years is a *disorder of personality* All writers are agreed that abnormal irritability spitefulness and occasional violence are a feature of the disease These tend to appear very early in the course and are periodic commonly on a background of mild but progressive apathy and loss of interest in home friends and occupation Bouts of mild depression occur with and independently of the periods of irritability and both may last hours or days at a time Euphoria is unusual elation or expansive delusions so rare as to lead to suspicion of other cause of precipitating factor A common early symptom is *anxiety* presenting itself either alone or in association with mild memory defect Lion and Kahn describe various anxiety reactions It is natural that a member of an affected family should fear the onset of the disease but our own experience of this symptom in patients who were unaware of the liability leads us to assume that it was a reaction to sense of incapacity not yet demonstrable objectively Diefendorf comments on a type of increasing apprehension leading to self accusation depression with occasional hallucinations of hearing considerable agitation and frequent suicidal attempts These disturbances are episodic and occasionally progress to delirium Alcohol

to every voluntary act, and although the patient may be able to stand still for a few moments, he cannot walk without little hesitations and unequal steps lurches this way and that, owing to unexpected movement of either limb The upper limbs are held out from the body, the fingers and hands moving in irregular oscillation, the head and trunk usually held stiffly as if in intent concentration in maintaining balance, in more severe degrees the gait is more grossly interrupted and finally impossible At this stage the patient has difficulty in sitting in a chair for fear that the movements of the arms and trunk will unbalance him The arms are alternately raised and lowered, flexed and extended, the head turned this way or that but often deeply flexed on the chest and as smoothly hyperextended, the lips protruded and turned to one or other side in an endless contortion The movements are not violent or incoordinate for they are easily prevented by passive resistance There is no conflict of antagonists and therefore no pain or cramp

Speech usually is affected early in the course of the disease but only in the periodic interruption by movements of the tongue and lips, which, by later becoming continuous lead eventually to incoherence Swallowing and respiration similarly are periodic in the later course

The involuntary movements are greatly increased in number and frequency by excitement and by attempt to perform an unusual or difficult voluntary movement They are lessened in repose and usually absent in sleep, except for some slight movements in restless states

It will be remarked that the movements differ only in more rapid speed of performance from those of double athetosis a relationship noted by Audry [3] and by Bonnet[331], who claimed that a number of transition cases between chorea and double athetosis occurred 'Double athetosis' is however, progressive in a different fashion and has a different pathology It is in the types of Huntington's chorea with progressive rigidity that movements identical with athetosis are to be expected Indeed the author regards the movements of Huntington's chorea as a variety of athetoid movement There is no real resemblance to Sydenham's chorea, myoclonus torsion spasm or the tremor of parkinsonism

The facial expression in repose however, often has a set, slightly staring appearance reminiscent of the "mask" of parkinsonism The muscles usually are hypotonic or offer only normal resistance to passive movement The few cases described in the literature as being rigid[95 315] have either exhibited this in an advanced stage of the disease or have been members of families in which a separate element of feeblemindedness has been present When present in an advanced stage the rigidity appears identical with that of parkinsonism Tremor is not a symptom of the disease

Apart from the involuntary movements the muscular system is unaffected,

Minski and Guttmann found psychopathic traits in many non choreic sibs but only very prolonged observation could determine whether these were not early signs of affection These authors also note that some affected members resembled the choreic ancestor in appearance and unaffected members resembled the unaffected parent The "choreopathic personality" of Kehrer [36] is a nebulous conception not clearly separated from the symptoms of the disease Such symptoms as slight twitchings nervous restlessness hasty speech and exaggerated gestures are indistinguishable from the early signs of the disease on the one hand or benign nervousness on the other and there is no real ground for their being regarded as the stigmata of the carrier of the disease as do Reisch and Fatzig [3, 8] The difficulty in assessing such studies is that Huntington's chorea cannot be regarded as necessarily steadily progressive in course for there are numerous examples of lack of progression of symptoms for many years If this can occur late in the disease it should also be possible in early stages as only good follow ups can prove conclusively If this is true the concept of the Vogts of a basic stationary structural smallness of the striatum in pre choreics is not valid

Pathology

In the early cases reported by Sinkler[1] and Osler[317] general atrophy of the cerebral convolutions was noted with an increased firmness on section Ganglion cells were noted by Osler to be sometimes vacuolated some laden with pigment There is no mention of the basal ganglia In 1908 Lannois and Paviot [3] noted that there was also chromatolysis and perivascular infiltration in the basal ganglia, but the most significant contribution was made in 1909 by Jelgersma [8] who described atrophic change in the head of the caudate nucleus which was reduced to one third of its usual size There was also marked proliferation of glia cells Alzheimer [1] in a pathological study of 3 cases found in addition to degenerative changes in the cortex advanced degeneration in the cells of both caudate and lenticular nuclei The striatal nerve cells were greatly reduced in number and with corresponding increase in glial nuclei without fibers He also found some evidence of cell degeneration in the subthalamic region thalamic nuclei and brain stem Some deposits of lipoid in both nerve cells and glia and in vessel walls were found also These changes were confirmed by Pfeiffer[3] who gives some excellent illustrations of degenerative changes in ganglion cells which he found most evident in frontal cortex and striatum especially putamen but also in less degree in other regions of the cortex and in the optic thalamus Marie and L'Hermitte[8, 1] in reporting 4 cases described in detail atrophy and gliosis of the frontal and immediate post central cortex The tangential myelin had disappeared in the frontal lobe and radiating fibers were sparse and poorly myelinated

ism is not infrequent and with dietary insufficiency and other possible toxic causes must be suspected in such states A number of advanced cases nevertheless present auditory hallucinations without evidence of other causes

Schizophrenic types of reaction are so rare as to be explained by coincidence and although a separate schizophrenic heredity has been found in some, such independence usually is not demonstrable[3 5] Paranoid symptoms are more common but as in other organic reaction states depend more on the patient s basic personality than on any peculiarity of the disease Alcoholism is common both in affected and unaffected members but is uneven in distribution and not necessarily associated with liability to subsequent chorea Criminal behavior is recorded occasionally but is rare considering the frequency of change in personality of which it can sometimes occur as first symptom A high frequency of *suicide* was recorded by Huntington and is mentioned by others since Davenport and Muncie report only o in 962 cases, and Minski and Guttmann[3] in reviewing the question point to the relatively low incidence in unaffected members of families of choreics and its occurrence often in an advanced stage of the disease when intellectual deterioration is already manifest It would, therefore, appear to be related to episodic impulsive behavior rather than to the fear of the disease on which Bell[315] laid stress

Pre morbid Personality

The eugenic difficulty which arises from the lateness of onset of the disease has been discussed by several writers Any method of recognition of an affected member of a family in adolescence undoubtedly would be of great value Early irritability and nervous and excitable disposition frequently is found in siblings who do not develop chorea and cannot be regarded as a reliable early sign[309 3 4] ' In a family characterized by irritability preceding onset of the disease the gradual or sudden appearance of this symptom some years before the usual age of onset should discourage marriage while the absence of excitability, irritability, restlessness or insomnia up to the age of 36 or 40 may usually be considered permissive — excepting in the most phlegmatic strains — of marriage "[3 9] A prospective spouse may be inclined to risk the chance of having to care for the mate but often does not appreciate the prospects of totally dependent children

Choreic families are more often than not successful and prosperous Davenport and Muncie[309] found 5 legislators, 1 judge, 2 university professors, 2 ministers 1 eminent surgeon 3 authors, 2 mechanical geniuses and 2 organizers of public institutions in his group of families some of whom became affected, some not Spillane and Phillips[335] found no mental or nervous abnormality in 152 non choreic relatives who were in general ' intelligent industrious and sober folk '

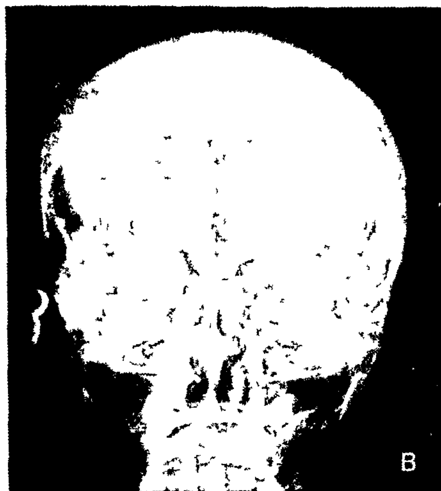


Fig 4 Pneumencephalograms of two cases of Huntington's Chorea

cord were found but were *not* constant The process was regarded as resulting from a *chronic* encephalitis or intoxication

These changes have been confirmed and extended in a number of studies by Kleist the Vogts Spielmeyer Jakob Dunlap and others and recently well reviewed by Stone and Falstein Bielschowsky confirmed the finding of Kisselbach the Vogts and others that the small cells of the caudate nucleus are the most severely damaged but found the larger cells qualitatively and quantitatively more severely affected in longer progress of the disease Later the ganglion

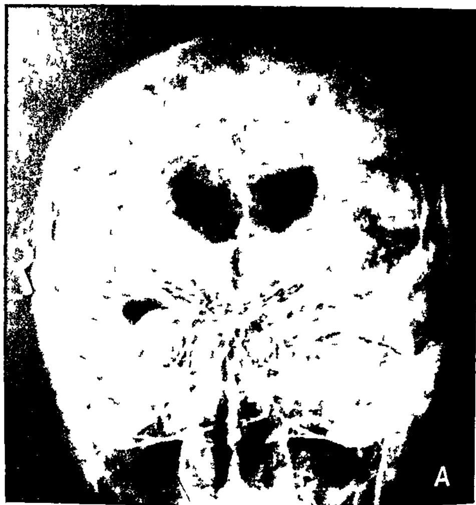


FIG 4 Pneumencephalograms of two cases of Huntington's Chorea

The cellular layers were altered profoundly with almost complete disappearance of the normal lamination in some areas Even the Betz cells showed changes The nuclei were displaced to one side and a large mass of yellow pigment filled the shrunken cell body There was gliosis throughout the cortex with satellitosis and some perivascular infiltration with round cells In 2 cases small foci of cortical necrosis were found

Cellular degeneration in the caudate and lenticular nuclei was severe in all 4 cases with great proliferation of fibrous astrocytes The pallidum was shrunken but did not suffer cell loss No degeneration of descending striatal fiber systems was found Mild degenerative changes in the cerebellum brain stem and spinal

Other Forms of Adult Chorea

A condition in which involuntary movements indistinguishable from Huntington's chorea appear after the fifth decade in persons without any family history of chorea or dementia and usually called "senile chorea" has long been known. It is not uncommon, tends to run a benign course and usually mental deterioration is mild or absent. Huet[1] and others before him regarded the condition as related to Sydenham's chorea. Osler[1], Entres[31] and most modern writers consider the condition as a sporadic variant of the hereditary form. In view of the lateness of onset a negative family history would only be valid if a substantial number of the "unaffected" members had reached an advanced age. Such a history usually is not obtainable. Autopsy findings reveal smallness of the caudate nucleus and putamen with cell changes identical with those of Huntington's chorea.[1] In a case described by Davidson and associates[1] siderosis of these nuclei was prominent, but the patient, who was aged 54, was described as having "a dystonic fragment in the foot", and in the absence of any details of the involuntary movements would appear to belong to the category of double athetosis with progressive rigidity described by Hallervorden and Spatz.

On account of the occurrence of isolated instances of chorea without family history with onset as early as 31 years, it appears desirable to recognize the occasional "sport" or "throw back", which according to Bell occurs also in other hereditary disease and is likened by Osler to sporadic cases of Friedreich's ataxia. Whether such cases always pass on the disease to their children is doubtful, but the 6 families in the literature with unaffected grandparents suggest that such is probable.

Of more uncertain significance is the occurrence of choreic movements as a transient event in the course of an acute infection, pregnancy or transient psychoses. Brissaud[1] named "variable chorea" the transitory appearance of choreic movements in mental defectives, either in adolescence or in middle life, in relation to episodic psychosis, and Lewis and Minski recently have commented on their appearance in the course of toxic psychosis, for example with acute streptococcal infections, in otherwise mentally stable adults. It is tempting to regard such a disturbance as Sydenham's chorea in an adult, but the symmetry of movement, the brevity of the attack and often the more fluid type of movement of Huntington type leave an impression of other relationship. Further, members of families liable to Huntington's chorea who later develop the disease sometimes give a history of choreic movements with a toxemia of pregnancy, and in others the onset of the disease is precipitated by pregnancy. No condition of striatal insufficiency is recognized, but the occurrence of such movements in relation to an infection in a patient who had suffered from icterus gravis neonatorum

cells of the pallidum also became affected and this nucleus could also shrink Finally, the strio subthalamic fibers were thinned, and degeneration of the corpus subthalamicum occurred as Alzheimer first observed The process of cellular degeneration according to Bielschowsky is extremely slow with accumulation of fat and pigment within the cell The glial reaction is the reaction to any secondary degeneration and is not specific in any way and does not deserve the title status fibrosus conferred by the Vogts [1] Dunlap [1] confirmed these findings with measurements of the loss in volume and cell count of the caudate and lenticular nuclei and beautiful illustrations of the gliosis Bielschowsky showed that in an early and progressive case with ultimate rigidity the globus pallidus was severely damaged although still not as severely as the striatum

Dunlap found the most severe affection in the posterior three fourth of the putamen and in the head of the caudate nucleus The shrinkage of these regions usually is clearly visible to the naked eye on section of the fresh brain Indeed in some cases there appears to be little of the caudate nucleus remaining a fact which can be very striking in an air encephalogram of the living patient when the rounded anterior horn of the lateral ventricle reveals the absence of caudate nucleus (Fig 4) By contrast Dunlap found no measurable thinning of the cerebral cortex although the brain is as a whole small and gliosis in the deeper layers of frontal cortex intense Most authors find the loss of cortical cells most severe in the middle layers, some in the deepest layers In some cases the occipital cortex is involved also The cerebellum, thalamus and brain stem nuclei including substantia nigra are spared even in rigid cases

The evidence of inflammatory reaction, meningeal thickening and pachymeningitis described by earlier authors is now regarded as resulting from complicating infections or trauma Some hyaline changes and obliterative arteritis are a constant accompaniment of the cortical and striatal lesion but is not regarded as primary

No visceral lesion has ever been demonstrated to accompany Huntington's chorea and the mechanism of the degenerative disorder remains as mysterious as its hereditary linkage

Treatment

The generalized and progressive nature of the disease and the lack of any information as to its mechanism deny any rational treatment Sedatives have little effect on the movements except in the continuance of undesirably large dosage of barbiturates It is generally agreed that palliative surgery is contraindicated in view of the course of the disease The difficulties in advice concerning marriage of apparently healthy relatives has been outlined in a previous paragraph

BIBLIOGRAPHY

1 DE BARENNE J G D CAROL H W and McCULLOCH W S Physiological neuronography of the cortico striatal connections Res Publ Assoc Nerv and Ment Dis 194 XXI 46

GLEES P The anatomical basis of cortico striate connexions Jour Anat 1944 LXXVIII 4,

3 RAMIREZ J W Reciprocal connections of the striatum and pallidum in the brain of Pitheus (Macacus) rhesus Jour Comp Neurol 1938 LXIX 3)

4 RAMIREZ J W A summary of the fiber connections of the basal ganglia with each other and with other portions of the brain Res Publ Assoc Nerv and Ment Dis 1942 XXI 1

5 METTLER F A Relation between pyramidal and extrapyramidal function Res Publ Assoc Nerv and Ment Dis 1942 XXI 150

6 TOWER S S The dissociation of cortical excitation from cortical inhibition by pyramid section and the syndrome of that lesion in the cat Brain 1935 LVIII 38 1936 LIX 408

, HUNT J R Progressive atrophy of the globus pallidus Brain 191, XL 58

8 METTLER F A Neuro anatomy Mo by Company St Louis 194

9 AYER J B and AITKEN H F Note on the arteries of the corpus striatum Boston Med and Surg Jour 190 CLVI 68

10 ALEXANDER L The vascular supply of the strio pallidum Res Publ Assoc Nerv and Ment Dis 194 XXI

11 RUBENSTEIN H S Relation of circulus arteriosus to hypothalamus and internal capsule Arch Neurol and Psychiat 1944 LII 5 6

1 ABBIE A A The clinical significance of the anterior choroidal artery Brain 1933 LVI 33

13 WILSON S A K Progressive lenticular degeneration a familial nervous disease associated with cirrhosis of the liver Brain 191 XXXIV 95

14 FULTON J F JACOBSEN C F and KENNARD M A A note concerning the relation of the frontal lobes to posture and forced grasping in monkeys Brain 193 LV 5 4

15 FULTON J F Physiology of the Nervous System nd ed Oxford University Press New York 1943

16 TOWER S S Pyramidal lesion in the monkey Brain 1940 LXIII 6

1 TOWER S S The pyramidal tract Chap 6 in The Precentral Motor Cortex editor P C Bucy Univ Illinois Press Urbana 1944

18 MAGNUS R Korperstellung Julius Springer Berlin 19 4

19 BIEBER I and FULTON J F Relation of the cerebral cortex to the grasp reflex and to postural and righting reflexes Arch Neurol and Psychiat 1938 XXXIX 433

o METTLER F A METTLER C C and CULLER E A Effects of total removal of the cerebral cortex Arch Neurol and Psychiat 1935 XXXIV 1 58

leads the author to believe that the mechanism of the chorea in such cases lies in a residual unstable state of the striatum existing since infancy

The *familial paroxysmal choreo athetosis reported by Mount and Reback*[346] occurred in attacks lasting up to four hours at a time in otherwise healthy individuals It appears to be more closely related to the paroxysms of torsion spasm of Wilson's disease than to Huntington's chorea and one patient was reported to show a Kayser Fleischer ring

In 1920 Creutzfeld and in 1921 Jakob described an ill defined disease for which the name ' *spastic pseudosclerosis* was suggested It is now generally known as the *Jakob Creutzfeld syndrome* the gradual onset in middle life of a progressive weakness and spastic stiffness of the lower limbs with mental deterioration In addition parkinsonian facies and tremors or athetoid movement and dysarthria and muscular atrophy may be present Most commonly the clinical picture is that of a presenile dementia with spasticity and fibrillation A heredo familial form is described The course of the disease is often rapid and leads to a fatal termination in about one year The pathology resembles that of Huntington s chorea with the addition of degeneration of the pallidum, the cortico spinal tracts and of anterior horn cells[34] Since the extra pyramidal signs and symptoms are either slight or absent and the present status of the disease uncertain[348], it is mentioned here only in differentiation from Huntington s chorea The condition has been reviewed recently by Wilson[1 3]

BIBLIOGRAPHY

1 DE BARENNE J G D CAROL H W and McCULLOCH W S Physiological neuronography of the cortico striatal connections Res Publ Assoc Nerv and Ment Dis 194 XXI 46

GLEES P The anatomical basis of cortico striate connexions Jour Anat 1944 LXXVIII 4

3 PAPEZ J W Reciprocal connections of the striatum and pallidum in the brain of Pitheus (Macacus) rhesus Jour Comp Neurol 1938 LXIX 3 9

4 PAPEZ J W A summary of the fiber connections of the basal ganglia with each other and with other portions of the brain Res Publ Assoc Nerv and Ment Dis 1942 XXI 21

5 METTLER F A Relation between pyramidal and extrapyramidal function Res Publ Assoc Nerv and Ment Dis 194 XXI 150

6 TOWER S S The dissociation of cortical excitation from cortical inhibition by pyramid section and the syndrome of that lesion in the cat Brain 1935 LVIII 238 1936 LIX 408

7 HUNT J R Progressive atrophy of the globus pallidus Brain 1917 XL 58

8 METTLER F A Neuro anatomy Mosby Company St Louis 1942

9 AYER J B and AITKEN H F Note on the arteries of the corpus striatum Boston Med and Surg Jour 190 CLVI 68

10 ALEXANDER L The vascular supply of the strio pallidum Res Publ Assoc Nerv and Ment Dis 1942 XXI 77

11 RUBENSTEIN H S Relation of circulus arteriosus to hypothalamus and internal capsule Arch Neurol and Psychiat 1944 LII 526

1 ABBIE A A The clinical significance of the anterior choroidal artery Brain 1933 LVI 233

13 WILSON S A K Progressive lenticular degeneration a familial nervous disease associated with cirrhosis of the liver Brain 191 XXXIV 95

14 FULTON J F JACOBSEN C F and KENNARD M A A note concerning the relation of the frontal lobes to posture and forced grasping in monkeys Brain 193 LV 524

15 FULTON J F Physiology of the Nervous System nd ed Oxford University Press New York 1943

16 TOWER S S Pyramidal lesion in the monkey Brain 1940 LXIII 36

17 TOWER S S The pyramidal tract Chap 6 in The Precentral Motor Cortex editor P C Bucy Univ Illinois Press Urbana 1944

18 MAGNUS R Korperstellung Julius Springer Berlin 1924

19 BIEBER I and FULTON J F Relation of the cerebral cortex to the grasp reflex and to postural and righting reflexes Arch Neurol and Psychiat 1938 XXXIX 433

0 METTLER F A METTLER C C and CULLER E A Effects of total removal of the cerebral cortex Arch Neurol and Psychiat 1935 XXXIV 1 38

1 BARD P and RIOCH D McK A study of four cats deprived of neocortex Bull Johns Hopkins Hosp 1937 LX 73

RIOCH D McK Certain aspects of the behavior of decorticate cats Psychiatry 1938 I 339

3 RIOCH D McK Neurophysiology of the corpus striatum and globus pallidus Psychiatry 1940 III 119

4 McCULLOCH W S Cortico cortical connections Chap 8 of The Precentral Motor Cortex editor P C Bucy Univ Illinois Press Urbana 1944

5 LEVIN P N The efferent fibers of the frontal lobe of the monkey (Macaca mulatta) Jour Comp Neurol 1936 LXIII 369

6 METTLER F A and METTLER C C Role of the neo triatum Am Jour Physiol 1941 CXXXIII 594

7 KENNARD M A and FULTON J F Corticostriatal interrelations in monkey and chimpanzee Res Publ Assoc Nerv and Ment Dis 194 XXI 8

8 WILSON S A K An experimental research into the anatomy and physiology of the corpus striatum Brain 1913–14 XXXVI 4 7

9 RANSON S W and BERRY C Observations on monkeys with bilateral lesions of the globus pallidus Arch Neurol and Psychiat 1941 XLVI 504

30 RIOCH D McK and BRENNER C Experiments on the corpus striatum and rhinencephalon Jour Comp Neurol 1938 LXVIII 491

31 SHERRINGTON C S Flexion reflex of the limb cro sed extension reflex and reflex stepping and standing Jour Physiol 1910 XL 8

32 LORENTE DE NO R Die Labyrinthreflexe auf die Augenmuskeln nach ein seitiger Labyrinthexstirpation Urban and Schwarzenberg Berlin 19 8

33 JACKSON J HUGHLINGS Selected Writings edited by J Taylor vol pp 58 453 Hodder and Stoughton London 193

34 COGHILL G E Correlated anatomical and physiological studies of the growth of the nervous system of amphibia Jour Comp Neurol 19 6 XL 47 19 6 XLI 95 1926 XLII 1 1931 LIII 147

35 COGHILL G E The early development of behavior in amblystoma and in man Arch Neurol and Psychiat 19 9 XXI 989

36 COGHILL G E Flexion spasms and mass reflexes in relation to the ontogenetic development of behavior Jour Comp Neurol 1943 LXXIX 463

37 BIELSCHOWSKY M Ueber Hemiplegia bei intakter Pyramidenbahn Jour Psychol u Neurol 1918 XXII 5

38 WILSON S A K and WALSHE F M R The phenomenon of tonic innervation and its relation to motor apraxia Brain 1914 XXXVII 199

39 CAZAUVIEILH J B Recherches sur l agenesie cerebrale et la paralysie congenitale Arch gen de Med 1827 XIV 5 and 347

40 HAMMOND W A A Treatise on Diseases of the Nervous System Appleton New York 1871

41 MITCHELL S WIER Post paralytic chorea Am Jour Med Sci 1874 LXVIII 34

4 GOWERS W R On athetosis and post hemiplegic disorders of movement Med Chir Trans 18,6 LI\ 1
43 SCHILDER P Ueber Chorea und Athetose Zeitschr f d ges Neurol u Psychiat 1911 VII 219
44 CHARCOT J M De l hemichoree post hemiplegique Prog med 18,5 III 69
45 MARTIN J P and ALCOCK N S Hemichorea associated with a lesion of the corpus luysii Brain 1934 LVII 504
46 MOERSCH F P and KERNOHAN J W Hemiballismus a clinicopathologic study Arch Neurol and Psychiat 1939 XLI 364
4, MARIE P and GUILLAIN G Lesion ancienne du noyau rouge Nouv Iconogr de la Salpetriere 1903 XVI 80
48 LANDOUZY L Note sur un cas d athetose Prog med 18 8 VI 9 and 96
49 DAVISON C and GOODHART S P Monochorea and somatotopic localisation Trans Am Neurol Assoc 65th Session pp 106–110 1939
50 WEIL A A contribution to the pathology of hemichorea Brain 1928 LI 36
51 VOGT C and VOGT O Zur Lehre der Erkrankungen des striaren Systems Jour f Psychol u Neurol 19 0 XXV 62, abstracted at some length by Winkelman Arch Neurol and Psychiat 19 3 X 563
52 FOERSTER O Zur Analyse und Pathophysiologie der striaren Bewegungsstorungen Zeitschr f d ges Neurol u Psychiat 19 1 LXXIII 1
53 BUCY P C Relation to abnormal involuntary movements Chap XV of The Precentral Motor Cortex editor P C Bucy Illinois Press Urbana 1944
54 GUILLAIN G and DUBOIS J Sur un cas d athetose avec signe de Babinski provoqne par l excitation de la surface cutanee de tout le corps Rev Neurol 1914 XXVII 714
55 ANDRÉ-THOMAS De la nature des mouvements choreiques Presse med 19 2 XXX 5
56 CATHALA J Rigiditee decerebree unilaterale avec attitude de torsion par tumeur thalamo pedunculaire Rev Neurol 19 XXXIX 1504
57 WILSON S A K Die Pathogenese der unwillkurlichen Bewegungen mit besonderer Berucksichtigung der Pathologie und Pathogenese der Chorea Deutsch Zeitschr f d Nervenheilk 19 9 CVIII 4
58 MAYENDORF N von Chorea und Linsenkern Monatschr f Psychiat u Neurol 1930 LXXIV 3
59 HOLMES G On certain tremors in organic cerebral lesions Brain 1904 XXVII 32,
60 VAN BOGAERT L and BERTRAND I Étude anatomo clinique d un syndrome alterne du noyan rouge avec mouvements involontaires rhythmes de l hemiface et de l avant bras Rev Neurol 193 I 38
61 VOGT C and VOGT O Erkrankungen der Grosshirnrinde im Lichte der Topistik Pathoklise und Pathoarchitektonik Jour Psychol u Neurol 1922 XXVIII 1
62 MEYER A Klinisch anatomische Erfahrungen uber Kohlenoxydvergiftung des Zentralnervensystems Klin Wochenschr 19 7 VI 145

63 HADFIELD G Siderosis of the globus pallidus its relation to bilateral necrosis Jour Path and Bact 1929 XXXII 135
64 MASSALONGO R Contribution a l origine corticale des tremblements Rev Neurol 1903 XI 455
65 VOGT C and VOGT O Sitz und Wesen der Krankheiten im Lichte der Topistischen Hirnforschung und des Variiens der Tiere Jour Psychol u Neurol 1936 XLVII 237
66 ERB W Paralysis Agitans (Parkinson s Disease) pp 880–898 in Modern Clinical Medicine Diseases of the Nervous System edited by Church transl from Die Deutsche Klinik Appleton London 1908
67 GOWERS W R Paralysis Agitans Vol 8 pp 473–48 in Allbutt and Rolleston s System of Medicine Macmillan London 1910
68 MENDEL K Die Paralysis Agitans S Karger Berlin 1911
69 HART T S Paralysis agitans some clinical observations based on the study of 19 cases seen at the clinic of Professor M Allen Starr Jour Neur and Ment Dis 1904 XXXI 177
70 PATRICK H T and LEVY D M Parkinson s disease a clinical study of one hundred and forty six cases Arch Neurol and Psychiat 19 VII 711
71 BELL J and CLARK A J A pedigree of paralysis agitans Am Eugenics 19 5–26 I 455
7 DELLAERT R NYSSEN R and VAN BOGAERT L La paralysie agitante a charactere hereditaire et familial Jour Belge de Neurol et de Psychiat 1937 XXXVII 747
73 KEHRER F Der Ursachenkreis des Parkinsonismus (Erblichkeit Trauma Syphilis) Arch f Psychiat 1930 XCI 187
74 PARKINSON J An Essay on the Shaking Palsy Sherwood Neely and Jones London 1817 reprinted with bibliographic note by A J Ostheimer Arch Neurol and Psychiat 192 VII 681 and Medical Clinics 1938 II 956
75 COHN B Ein Beitrag zur Lehre der Paralysis Agitans Wien med Wochenschr 1860 X 73 289 305 388 and 406
76 ORDENSTEIN L Sur la paralysie agitante et la sclerose en plaques generalisee These de Paris E Martinet Paris 1867
77 MANSCHOT G W Paralysis Agitans Psychiat Neurol Bl den Amst 1904 VIII 597
78 JELGERSMA G Neue anatomischen Befunde bei Paralysis Agitans und bei chronischer Chorea Zentbl f Neurol 1908 XXVII 995
79 LEWY F H Die pathologische Anatomie der Paralysis Agitans Lewandowsky s Handb 191 III 9 0 and Deutsch Zeitschr f Nervenheilk 1913 L 50
80 BRISSAUD E Leçons sur les Maladies Nerveuses ed by H Meige Masson Paris 1895
81 COBB S Electromyographic studies of paralysis agitans Arch Neurol and Psychiat 19 VIII 47

82 HOEFER P F A Physiology of motor innervation in the dyskinesias Res Publ Assoc Nerv and Ment D 1942 XXI 50
83 INGEBRIGHTSEN B Practical application of electromyography in diagnosis of tremor Acta Psychiat et Neurol 1938 XIII 11
84 FOIX C and THEVENARD A Relachement paradoxicale au cours de mouvement volontaire de certains muscles agonistes ou antagonistes chez un sujet atteint de maladie de Parkinson Rev Neurol 19 XXXIX 56
85 LYONS L V and BRICKNER R M Physiologic differences between generic and individually acquired automatic associated movements Arch Neurol u Psychiat 1931 XXV 398
86 WILSON S A K Modern Problems in Neurology Arnold London 19 8 and Croonian Lectures Lancet 19 5 II 1 53 169 15 and 68
87 WALSHE F M R Observations on the nature of the muscular rigidity of paralysis agitans and on its relationship to tremor Brain 19 4 XLVII 159
88 BECHET E Note sur quelques attitudes rares observees dans la maladie de Parkinson Nouv Iconogr de la Salpetriere 189 V 3
89 RICHER P and MEIGE H L habitus exterieur dans la maladie de Parkinson Nouv Iconogr de la Salpetriere 1895 VIII 361
90 SANDS I J The type of personality susceptible to Parkinsons disease Jour Mount Sinai Hosp 194 IX 9
91 OPPOLZER J R Fall von Paralysis agitans Wien med Wochenschr Beilage Spitals Zeitung 1861 CCXLIX 6
92 LEWY F H Zur pathologisch anatomischen Differentialdiagnose der Paralysis agitans und der Huntingtonschen Chorea Zeitschr f d ges Neurol u Psychiat 19 1 LXXIII 1 0
93 LEWY F H Die Lehre vom Tonus und Bewegung Monogr ges Neurol u Psychiat Foerster Wilmanns Heft 34 Springer Berlin 1923
94 TRETIAKOFF C Contribution a l etude de l anatomie pathologique du locus niger de Soemmering These de Paris No 93 Jouve et Cie Paris 1919
95 BIELSCHOWSKY M Weitere Bemerkungen zur normalen und pathologischen Histologie des striaren Systems Jour f Psychol u Neurol 19 2 XXVII 33
96 LHERMITTE J and CORNIL L Recherches anatomiques sur la maladie de Parkinson Rev Neurol 19 1 XXXVII 189 and 587
97 FOIX M C Les lesions anatomiques de la maladie de Parkinson Rev Neurol 1921 XXXVII 593
98 JACOB A Die Extrapyramidalen Erkrankungen J Springer Berlin 19 3 abstr at length by author Arch Neurol and Psychiat 19 5 XIII 596
99 KESCHNER M and SLOANE P Encephalitic idiopathic and arteriosclerotic parkinsonism Arch Neurol and Psychiat 1925 XXV 1011
100 DAVISON C The role of the globus pallidus and substantia nigra in the production of rigidity and tremor Res Publ Assoc Nerv and Ment Dis 194 XXI 67
101 HALLERVORDEN J Anatomische Untersuchungen zur Pathogenese des post Vor XI 1 45

encephalitischen Parkinsonismus Deutsch Zeitschr f Nervenheilk 1935-6 CXXXVI 68
10 NEUSTAEDTER M and LIBER A F Concerning the pathology of parkinsonism (idiopathic arteriosclerotic and postencephalitic) Jour Nerv and Ment Dis 1937 LXXXVI 64
103 BENDA C E and COBB S On the pathogenesis of paralysis agitans (Parkinson s disease) Medicine 194 XXI 95
104 DILLENBERG S M MERRITT H H PRICE J C and Associates The treatment of paralysis agitans with drugs Res Publ Assoc Nerv and Ment Dis 1942 XI 54
105 VOLLMER H Comparative value of solenaceous alkaloids in the treatment of Parkinson s syndrome Arch Neurol and Psychiat 194 XLVIII ,
106 WILLIGE H Ueber Paralysis agitans im jugendlichen Alter Zeitschr f d ges Neurol u Psychiat 1911 IV 520
107 VAN BOGAERT L Contribution clinique et anatomique a l etude de la paralysie agitante juvénile primitive Rev Neurol 1930 II 315
108 HALL H C La Degenerescence Hepato lenticulaire Masson et Cie Paris 19 1
109 WIMMER A Chronic Epidemic Encephalitis Heinemann London 19 4
110 HALL A Epidemic Encephalitis (Encephalitis Lethargica) Wm Wood Co London and New York 19 4
111 VON ECONOMO C Encephalitis Lethargica its Sequelae and Treatment Trans by K O Newman Oxford Univ Press London 1931
112 WILSON S A K Neurology Vol 1 Chapt VIII Arnold London 1940
113 MATHESON COMMISSION Epidemic Encephalitis Etiology Epidemiology Treatment Columbia Univ Press New York 19 9
114 MATHESON COMMISSION Epidemic Encephalitis second report Columbia University Press New York 1932
115 TILNEY F and HOWE H S Epidemic Encephalitis Hoeber New York 19 0
116 NEEL A V On atypical and masked forms of encephalitis epidemica (lethargica) Jour Nerv and Ment Dis 19 6 LXIII 1
117 LUCKSCH F and SPATZ H Die Veranderungen im Zentralnervensystem bei Parkinsonismus in den Spatstadien der Encephalitis epidemica Munch med Wochenschr 1924 LXX 1 45
118 HOHMAN L Pathologisch anatomische Untersuchungen uber den encephalitischen Parkinsonismus Arch d Neurol Instit Wien Univers 1925 XXVII 1
119 SPATZ H Die Substantia nigra und das extrapyramidal motorische System Deutsch Zeitschr f Nervenheilk 1923 LXXVII ,5
120 McALPINE D The anatomico pathological basis of the parkinsonian syndrome following epidemic encephalitis Brain 19 6 XLIX 525
1 1 BUCY P C Cortical extirpation in the treatment of involuntary movements Res Publ Assoc Nerv and Ment Dis 194 XXI 551
122 KLEMME R M Surgical treatment of dystonia with report of one hundred cases Res Publ Assoc Nerv and Ment Dis 194 XXI 596

123 MEYERS R The modification of alternating tremors rigidity and festination by surgery of the basal ganglia Res Publ Assoc Nerv and Ment Dis 194 XXI 602

124 PUTNAM T J The operative treatment of diseases characterized by involuntary movements (tremor athetosis) Res Publ Assoc Nerv and Ment Dis 1942 XXI 666

125 POOLE J L cited by Putnam 124

126 PUTNAM T J Treatment of unilateral paralysis agitans by section of the lateral pyramidal tract Arch Neurol and Psychiat 1940 XLIV 950

127 CRITCHLEY M Arteriosclerotic parkinsonism Brain 19 9 LII

128 MARIE P Foyers lacunaires de desintegration et differents autres etats cavitaires du cerveau Rev Medecine 1901 XXI 81

129 FOERSTER O Die arteriosklerotische Muskelstarre Allg Zeitschr f d Psychiat 1909 LXVI 90

130 COLLINS J A definite clinical variety of cerebral arteriosclerosis Jour Nerv and Ment Dis 1906 XXXIII 50

131 HURST E W On the so-called calcification in the basal ganglia of the brain Jour Path and Bact 19 6 XXIX 65

132 WILSON S A K and COBB S Mesencephalitis Syphilitica Jour Neurol and Psychopathol 19 4 V 44

133 WOHLFAHRT S S Pallido striare Symptome bei Lues in den basalen Ganglien des Gehirns Zeitschr f d ges Neurol u Psychiat 19 CVIII 115

134 WILSON S A K Neurology Vol I p 483 Arnold London 1940

135 MELLA H and KATZ S E Neurosyphilis as an etiological factor in the parkinsonian syndrome Jour Nerv and Ment Dis 19 4 LIX 5

136 NIELSEN J M and INGHAM S D Change of personality as a sequel of carbon monoxide poisoning Bull Los Angeles Neurol Soc 1940 V 185

137 GRINKER R R Parkinsonism following carbon monoxide poisoning Jour Nerv and Ment Dis 19 6 LXIV 18

138 SHILLITO F H DRINKER C K and SHAUGHNESSY T J The problem of nervous and mental sequelae in carbon monoxide poisoning Jour Am Med Assoc 1936 CVI 669

139 NIELSEN J M Carbon monoxide parkinsonism with recovery after three years Bull Los Angeles Neurol Soc 1943 VIII

140 BRZEZICKI E Der Parkinsonismus symptomaticus 5 Mitteilung Zur Frage des Parkinsonismus bei der Kohlenoxydvergiftung Arbeit aus Neurol Inst Univ Wien 1930 XXXII 148 (quoted by Alexander 141)

141 ALEXANDER L The fundamental types of histologic changes encountered in cases of athetosis and paralysis agitans Res Publ Assoc Nerv and Ment Dis 194 XXI 334

142 BUMKE O and KRAPF E Exogene Vergiftungen des Nervensystems in Bumke Foerster Handbuch der Neurologie Vol 13 J Springer Berlin 1936

143 HILLER F Ueber die krankhaften Veranderungen im Zentralnervensystem Vol VI 1 45

nach Kohlenoxydvergiftung Zeitschr f d ges Neurol u Psychiat 1924 XCIII 594
144 LEWEY F H and DRABKIN D L Experimental chronic carbon monoxide poisoning of dogs Am Jour Med Sci 1944 CCVIII 502
145 CHARLES J R Manganese toxaemia with special reference to the effects of liver feeding Brain 19 , L 30
146 FLINTZER A Ueber gewerbliche Manganvergiftung Arch f Psychiat 1931 XCIII 84
147 GAYLE R F Manganese poisoning and its effect on the central nervous system Jour Am Med Assoc 1925 LXXXV 2008
148 EDSALL D L WILBUR E I and DRINKER C K The occurrence cause and prevention of chronic manganese poisoning Jour Industr Hyg 1919 I 183
149 VOSS H Manganese intoxication Arch Gewerbepathol 1939 IX 453 abstr Jour Am Med Assoc 1939 CXIII 1845
150 CANAVAN M M COBB S and DRINKER C K Chronic manganese poisoning report of a case with autopsy Arch Neurol and Psychiat 1934 XXXIII 501
151 MELLA H The experimental production of basal ganglion symptomatology in macacus rhesus Arch Neurol and Psychiat 1924 XI 405
15 HURST E W and HURST P E The aetiology of hepato lenticular degeneration experimental liver cirrhosis Jour Path and Bact 1928 XXXI 303
153 NEGRO F Les syndromes parkinsoniens dans l intoxication sulfocarbonee Revue neurol 1930 XXXVII 518
154 SCHMORL Gehirn bei Blausaurevergiftung Munch med Wochnschr 19 0 LXVII 913
155 COURVILLE C B Untoward Effects of Nitrous Oxide Anesthesia Pacific Press Mountain View Calif 1939
156 KASIN E and PARKER S Momentary death and choreo athetosis following nitrous oxide anesthesia with recovery Arch Neurol and Psychiat 194 XLVII 45
157 KREISS P Ueber hereditaren Tremor Deutsch Zeitschr f Nervenheilk 191 XLIV 111
158 FERNET C Des tremblements These de Paris Asselin Paris 18,
159 LÜTHY F Ueber die hepato lentikulare Degeneration (Wilson Westphal Strumpell) Deutsch Zeitschr f Nervenheilk 1931 CXXIII 101
160 CASSIRER R Ein Fall von progressiver Linsenkernerkrankung Zentbl f Neurol 1913 XXXII 1284
161 BIELSCHOWSKY M and HALLERVORDEN J Symmetrische Einschmelzungsherde im Stirnhirn beim Wilson Pseudosklerosekomplex Jour f Psychol u Neurol 1931 XLII 17,
62 HUNT J R The striocerebellar tremor a study of the nature and localisation of the combined form of organic tremor Arch Neurol and Psychiat 19 VIII 664

163 SPILLER W The family form of pseudosclerosis and other conditions attributed to the lenticular nucleus Jour Nerv and Ment Dis 1916 XLIII 23
164 HOWARD C P and ROYCE C E Progressive lenticular degeneration associated with cirrhosis of the liver (Wilson's disease) Arch Int Med 1919 XXIV 49
165 WESTPHAL C Ueber eine dem Bild der cerebrospinalen grauen Degeneration aehnliche Erkrankung des centralen Nervensystems ohne anatomischen Befund nebst einigen Bemerkungen uber paradoxe Contraction Arch f Psychiat 1883 XIV 8
166 STRUMPELL A Ueber die Westphalsche Pseudosklerose und ueber diffuse Hirnsklerose insbesondere bei Kindern Deutsch Zentbl f Nervenheilk 1898 XII 115
167 STRUMPELL A Ein weiterer Beitrag zur Kenntnis der sog Pseudosklerose Deutsch Zentbl f Nervenheilk 1899 XIV 348
168 GOWERS W Diseases of the Nervous System Vol p 656 London 1888 and On tetanoid chorea and its association with cirrhosis of the liver Rev Neurol and Psychiat 1906 IV 49
169 HOMEN E A Eine eigenthumliche Familienkrankheit unter der Form einer progressive Dementia mit besonderen anatomischen Gefund Zentbl f Neurol 1890 IX 514
170 ORMEROD J A Cirrhosis of the liver in a boy with obscure and fatal nervous symptoms St Barth Hosp Reports 1890 XXVI 57
171 FLEISCHER B Die periphere braun grunliche Hornhauterfarbung als Symptom einer eigenartigen Allgemeinerkrankung Munch med Wochenschr 1909 LVI 1120
17 VOLSCH M Beitrag zur Lehre von der Pseudosklerose (Westphal Strumpell) Deutsch Zeitschr f Nervenheilk 1911 XLII 335
173 WILSON S A K Neurology Vol Arnold London 1940
174 HOLLOWAY T B Peripheral pigmentation of the cornea associated with symptoms simulating multiple sclerosis Am Jour Med Sci 1914 CXLVIII 55
175 THOMAS J J A report of three cases of chronic progressive lenticular degeneration with mental deterioration Jour Nerv and Ment Dis 1917 XLV 3 1
176 HOSSLIN C and ALZHEIMER A Ein Beitrag zur Klinik und pathologis h n Anatomie der Westphal Strumpell schen Pseudosklerose Zeitschr f d ges Neurol u Psychiat 1912 VIII 183
177 STOCKER W Ein Fall von fortschreitender Lenticulardegeneration Zeitschr f d ges Neurol u Psychiat 1913 XV 251
178 STOCKER W Anatomischer Befund bei einem Fall von Wilsonscher Krankheit (progressive Lenticulardegeneration) Zeitschr f d ges Neurol u Psychiat 1914 XXV 17
179 FLEISCHER B Ueber eine der Pseudosklerose nahestehende bisher unbekannte Krankheit gekennzeichnet durch Tremor psychiche Storung braunliche Pigmentierung bestimmter Gewebe insbesondere auch der Hornhaut

nach Kohlenoxydvergiftung Zeitschr f d ges Neurol u Psychiat 19 4 XCIII 594
144 LEWEY F H and DRABKIN D L Experimental chronic carbon monoxide poisoning of dogs Am Jour Med Sci 1944 CCVIII 502
145 CHARLES J R Manganese toxaemia with special reference to the effects of liver feeding Brain 19 7 L 30
146 FLINTZER A Ueber gewerbliche Manganvergiftung Arch f Psychiat 1931 XCIII 84
147 GAYLE R F Manganese poisoning and its effect on the central nervous system Jour Am Med Assoc 1925 LXXXV 008
148 EDSALL D L WILBUR E I and DRINKER C K The occurrence cause and prevention of chronic manganese poisoning Jour Industr Hyg 1919 I 183
149 VOSS H Manganese intoxication Arch Gewerbepathol 1939 IX, 453 abstr Jour Am Med Assoc 1939 CXIII 1845
150 CANAVAN M M COBB S and DRINKER C K Chronic manganese poisoning report of a case with autopsy Arch Neurol and Psychiat 1934 XXXIII 501
151 MELLA H The experimental production of basal ganglion symptomatology in macacus rhesus Arch Neurol and Psychiat 1924 XI 405
152 HURST E W and HURST P E The aetiology of hepato lenticular degeneration experimental liver cirrhosis Jour Path and Bact 1928 XXXI 303
153 NEGRO F Les syndromes parkinsoniens dans l intoxication sulfocarbonée Revue neurol 1930 XXXVII 518
154 SCHMORL Gehirn bei Blausaurevergiftung Munch med Wochnschr 19 0 LXVII 913
155 COURVILLE C B Untoward Effects of Nitrous Oxide Anesthesia Pacific Press Mountain View Calif 1939
156 KASIN E and PARKER S Momentary death and choreo athetosis following nitrous oxide anesthesia with recovery Arch Neurol and Psychiat 194 XLVII 45
157 KREISS P Ueber hereditaren Tremor Deutsch Zeitschr f Nervenheilk 191 XLIV 111
158 FERNET C Des tremblements These de Paris Asselin Paris 187
159 LUTHY F Ueber die hepato lentikulare Degeneration (Wilson Westphal Strumpell) Deutsch Zeitschr f Nervenheilk 1931 CXXIII 101
160 CASSIRER R Ein Fall von progressiver Linsenkernerkrankung Zentbl f Neurol 1913 XXXII 1284
161 BIELSCHOWSKY M and HALLERVORDEN J Symmetrische Einschmelzungsherde im Stirnhirn beim Wilson Pseudosklerosekomplex Jour f Psychol u Neurol 1931 XLII 177
162 HUNT J R The striocerebellar tremor a study of the nature and localization of the combined form of organic tremor Arch Neurol and Psychiat 19 VIII 664

199 BRIDGMAN O and SMYTH F S Progressive lenticular degeneration Jour Nerv and Ment Dis 1944 XCIX 534

200 SWEET W H GRAY S J and ALLEN J G Clinical detection of hepatic disease in hepato lenticular degeneration Jour Am Med Assoc 1941 CXVII 1613

201 HADFIELD G On hepato lenticular degeneration with the account of a case and the pathological findings Brain 1923 XLVI 147

202 BIELSCHOWSKY M and FREUND C S Ueber Veranderung des Striatums bei tuberoeser Sclerose und deren Beziehungen zu den Befunden bei anderen Erkrankungen dieses Hirnteiles Jour f Psychol u Neurol 1918 XXIV o

203 DEMOLE V and REDALIE L Syndromes extrapyramidaux apparentes a la degenerescence hepato lenticulaire Rev Neurol 192 XXXVIII 1 48

204 VAN WOERKOM W La cirrhose hepatique avec alterations dans les centres nerveux evoluant chez des sujets d age moyen Nou Iconogr de la Salpetriere 1914 XXVII 43

205 VON ECONOMO C and SCHILDER P Eine der Pseudosclerose nahestehende Erkrankung im Praesenium Zeitschr f d ges Neurol u Psychiat 19 o LV 1

206 LEVI L Troubles Nerveux d Origine Hepatique (Hepato Toxhemie Nerveuse) These de Paris No 15 A selin et Houzeau Paris 1896

207 VAN BOGAERT L and LEY R A Sclerose laterale paratypique d Erb Jour Neurol et Psychiat Belge 19 , XXVII 93

208 HURST E W and HURST P E The aetiology of hepato lenticular degeneration experimental liver cirrhosis poisoning with manganese chloroform phenylhydrazine bile and guanidin Jour Path and Bact 19 8 XXXI 304

209 CULLINAN E B Idiopathic jaundice (often recurrent) associated with subacute necrosis of the liver St Barth Hosp Reports 1936 LXIX 55

210 MAHAIM I La degenerescence hepato lenticulaire etude clinique anatomique et experimentale Schweiz Arch Neurol 19 5 XVI 252 1925–6 XVII 43 and 83

211 POLLAK E Ueber experimentelle Encephalitis Arb a d Neurol Instit Wien Univers 19 XXIII Heft 1

212 SCHALTENBRAND G Ueber einen Fall von Chorea mit Lebercirrhose Deutsch Zeitschr f Nervenheilk 19 6 XCI 1 4

213 McHENRY E W and PATTERSON J M Lipotropic factors Physiol Rev 1944 XXIV 128

214 EARLE D P and VICTOR J Cirrhosis of the liver caused by excess dietary cystine Jour Exp Med 1941 LXXIII 161

215 LILLIE R D and ASSOCIATES Cirrhosis of the liver in rats on a deficient diet and the effect of alcohol *Pub Health Rep Wash 1941 LVI 1255*

216 DIMITZ L and VUJIC V Zur Kenntnis der Pseudosklerose (Westphal Strumpell) Wien klin Wochenschr 19 5 XXXVIII 951 and 991

217 FUCHS A Experimentelle Enzephalitis Wien med Wochenschr 1921 LXXI 710

peripherie Lebercirrhose Deutsch Zeitschr f d Nervenheilk 191 XLIV 174
180 SPIELMEYER W Die histopathologische Zusammenhorigkeit der Wilson schen Krankheit und der Pseudosklerose Zeitschr f d ges Neurol Psychiat 19 0 LVII 312
181 POLLOCK L J The pathology of the nervous system in a case of progressive lenticular degeneration Jour Nerv and Ment Dis 191, XLVI 401
18 THOMALLA C Ein Fall von Torsionsspasmus mit Sektionsbefund und seine Beziehung zur Athetose double Wilsonschen Krankheit und Pseudosklerose Zeitschr f d ges Neurol u Psychia 1918 XLI 311
183 BIELSCHOWSKY M Entwurf eines Systems der Heredodegenerationen des Zentralnervensystems einschliesslich der zugehoerigen Striatumerkrankungen Jour f Psychiat u Neurol 1918 XXIV 48
184 WIMMER A Études sur les syndromes extra pyramidaux spasme de torsion progressif infantile Rev Neurol 19 1 XXXVII 06
185 WIMMER A Le spasme de torsion Rev Neurol 19 9 I 904
186 SPILLER W G Acquired double athetosis dystonia lenticularis Arch Neurol and Psychiat 19 0 IV 370
187 KEHRER F Zur Aetiologie und Nosologie der Pseudosklerose Westphal Wilson Zeitschr f ges Neurol u Psychiat 1930 CXXIX 488
188 DE LISI L Sulla malattia del Wilson Riv Patol Nerv Ment 19 9 XXXIV 1
189 LHERMITTE J and MUNCIE W S Hepatolenticular degeneration a report of three unusual cases Arch Neurol and Psychiat 1930 XXIII 750
190 GOODHART S P and BALSER B H Somatotopic localisation in the extra pyramidal system Arch Neurol and Psychiat 1938 XXXIX 1043
191 BARNES S and HURST E W Hepato lenticular degeneration Brain 19 5 XLVIII 79 19 6 XLIX 36 and 19 9 LII 1
192 VON ECONOMO C Wilson s Krankheit und das Syndrome du Corps strie" Zeitschr f d ges Neurol u Psychiat 1919 XLIII 173
193 MEESMANN A Ueber Pigmentation des Limbus corneae bei Morbus Addisonii Klin Monatsbl f Augenheilk 19 0 LXX 316
194 JACKSON J A and IMMERMAN S L A case of pseudosclerosis associated with a psychosis Jour Nerv and Ment Dis 1919 XLIX 5
195 SIEMERLING E and JAKOB A Klinischer und anatomischer Beitrag zur Lehre von der Pseudosklerose Westphal Strumpell mit Cornealring und doppelseitiger Scheinkatarakt (Spatfall) Deutsch Zeitschr f Nervenheilk 1931- CXXIII 18
196 McARDLE M J Wilson s disease with Kayser Fleischer ring Proc Royal Soc Med Lond 1936-, XXX 858
197 MARCHAND L and COURTOIS A De l epilepsie dite sous corticale ' striee ou extra pyramidale Rev Neurol 19 9 II 31
198 WEATHERLY H Progressive lenticular degeneration with electroencephalogram and pneumoencephalogram Am Jour Roentgenol 1941 XLV 714

238 GOODHART S I and KRAUS W M On the deformity of the foot in dystonia musculorum Arch Neurol and Psychiat 19 4 XI 436
239 DAVISON C and GOODHART S I Dystonia musculorum deformans a clini copathological study Arch Neurol and Psychiat 1938 XXXIX 939
240 VAN WOERKOM W Sur le role de la dystonie dans la desorganisation des mouvements volontaires Nouv Iconogr de la Salpetriere 1916–17 XXVIII 37
41 CASSIRER R and BIELSCHOWSKY M Halsmuskelkrampf und Torsion psmus Zeitschr f d ges Neurol u Psychiat 19 XXXIII 513
4 NIELSEN J M Autopsy in a case of dystonia musculorum deformans Bull Los Angeles Neurol Soc 1941 VI 87
243 DIMITRI V Un caso de distonia muscular deformante estudio anatomo clinico Semana med 193 I 428
44 GOZZANO M Atetosi doppia con rigidità progre siva Riv Neurol 1934 VII 1
245 DIMITRI V Segunda observación anátomo clínica de distonia muscular defor mante Semana med 1935 I
46 MEYER A and COOK L C État marbre Jour Neurol and Psychopathol 1936 XVI 341
4 HODSKINS M B and YAKOLEV P I Neurosomatic deterioration in epilepsy Arch Neurol and Psychiat 1932 XXVII 113
48 BURMAN M S Curare therapy for the release of muscle spasm and rigidity in spastic paralysis and dystonia musculorum deformans Jour Bone and Joint Surg 1938 XX 754
49 PUTNAM T J Treatment of athetosis and dystonia by ection of extrapyrami dal motor tracts Arch Neurol and Psychiat 1933 XXIX 504 1938 XXXIX 256
50 LITTLE W J On the influence of abnormal parturition difficult labours pre mature birth and asphyxia neonatorum on the mental and physical condition of the child especially in relation to deformities Trans Obstet Soc Lond 186 III 293
251 SHAW T C On athetosis or imbecility with ataxia St Barth Hosp Rep 18 3 IX 130
25 OULMONT P Étude Clinique sur l Atheto e Delahaye Paris 1878
53 AUDRY J L Athetose Double et les Chorees Chroniques de l Enfance Baillère Paris 1892
254 OSLER W The Cerebral Palsies of Children Blakiston Philadelphia 1889
255 MICHAILOWSKI D I Étude clinique sur l athetose double Nouv Icono r de la Salpetriere 1892 V 57 and 29
256 BERNHARD H Ueber Athetose Inaug Diss Wurzburg 1884 cited by Audry [52]
257 DEJERINE J and SOLLIER P Premier cas d athétose double datant de la premiere enfance Bull Soc Anat de Paris 1888 LXIII 601
258 FREUD S Die infantile Cerebrallähmung in Nothnagel s Specielle Pathologie und Therapie Band IX Th III Holder Wien 1897

218 WALSH M N Hepato lenticular degeneration Proc Staff Meet Mayo Clinic 1936 XI 757
219 SCHWALBE M W Eine Eigentumliche Tonische Krampform mit Hysterischen Symptomen Inaug Dissert G Schade Berlin 1908
220 ZIEHEN T Fall von tonischer Torsionsneurose Zentbl f Neurol 1911 XXX 109
221 OPPENHEIM H Ueber eine eigenartige Krampfkrankheit des kindlichen und jugendlichen Alters Zentbl f Neurol 1911 XXX 309
222 FLATAU E and STERLING W Progressive Torsionsspasmus bei Kindern Zeitschr f d ges Neurol u Psychiat 1911, VII 586
223 FRAENKEL J Dysbasia lordica progressiva dystonic musculorum deformans – tortipelvis Jour Nerv and Ment Dis 1912 XXXIX 361
224 HUNT J R The progressive torsion spasm of childhood (dystonic musculorum deformans) Jour Am Med Assoc 1916 LXVII 1430
225 JAKOB A Zur Frage der nosologischen und lokalisatorischen Auffassung der torsiondystonischen Krankheitserscheinungen Deutsch Zeitschr f Nervenheilk 193 CXXIV 148
226 MENDEL K Torsionsdystonie in Bumke Foerster Handbuch der Neurologie Vol 16 pp 848–870 J Springer, Berlin 1936
227 HERZ E Dystonia Arch Neurol and Psychiat 1944 LI 305 and 319 1944 LII 20
228 SPILLER W G A case of dystonia musculorum deformans Jour Nerv and Ment Dis 1913 XL 529
229 CASSIRER R Halsmuskelnkrampf und Torsionspasmus Klin Wochenschr 19 2 VI 53
230 ALPERS B J and DRAYER C S The organic background of some cases of spasmodic torticollis report of case with autopsy Am Jour Med Sci 1937 CXCIII 378
231 POTTS C S A case of hemiplegia in a child with unusual spasmodic movements Arch Neurol and Psychiat 19 0 IV 241
23 LWOFF CORNIL L and TARGOWLA R Spasme de torsion (dystonie lenticulaire) d origine infectieuse Rev Neurol 19 XXXVIII 14 9
233 WECHSLER I S and BROCK S Dystonia musculorum deformans Arch Neurol and Psychiat 19 VIII 538
234 BROCK S and WECHSLER I S Involuntary movements their unusual association and relation to the phenomenon of decerebrate rigidity Arch Neurol and Psychiat 1924 XI 698
235 MARIE P and FOIX C Les syncinésies des hemiplegiques Rev Neurol 1916 I 3 1916 II 145 and 6 0
236 WIMMER A Études sur les syndromes extra pyramidaux III Hemi syndromes syphilitiques Rev Neurol 19 2 XXXVIII 38
237 WIMMER A Études sur les syndromes extra pyramidaux spasme de torsion infantile debutant par crises d hemispasmes toniques (epilepsie striee) Rev Neurol 1925 II 81

,9 BUCY P C Cortical extirpation in the treatment of involuntary movements Res Publ Assoc Nerv and Ment Dis 1942 XXI 551
80 KLEMME R M Surgical treatment of dystonia with report of one hundred cases Res Publ Assoc Nerv and Ment Dis 1942 XXI 596
81 NAFFZIGER H Discussion of Bucy's paper [78] Arch Neurol and Psychiat 1937 XXXVII 101,
8 AMMOSOW M M Zur pathologischen Anatomie der pallidaren Formen von Athetose Jour f Psychol u Neurol 1931 XLI 374
83 FISHER O Zur Frage der anatomischen Grundlage der Athetose double und der posthemiplegischen Bewegungstorungen uberhaupt Zeitschr f d ges Neurol u Psychiat 1911 VII 463
84 ROTHMANN M Demonstration zu den Zwang bewegungen des Kindesalters Zentbl f Neurol 1915 XXXIV 444
85 HALLERVORDEN J and SPATZ H Eigenartige Erkrankung im extrapyramidalen System mit besonderer Beteiligung des Globus Pallidus und der Substantia Nigra Ein Beitrag zu den Beziehungen zwischen diesen beiden Zentren Zeitschr f d ges Neurol u Psychiat 19 2 LXXIX 254
286 KALINOWSKY L Familiare Erkrankung mit besonderer Beteiligung der Stammganglion Monatschr f Psychiat 1927 LXVI 168
8, HURST E W On the so called calcification in the basal ganglia of the brain Jour Path and Bact 1926 XXIX 65
288 HELFAND M Status pigmentatus its pathology and its relation to Hallervorden Spatz disease Jour Nerv and Ment Dis 1935 LXXXI 66
89 OSMAN M and SCHUKRU I Beitrag zur Histopathologie der Hallervorden Spatzschen Erkrankung Deutsch Zeitschr f Nervenheilk 1935 CXXXVI 78
90 WOODS A H and PENDLETON L Fourteen simultaneous cases of an acute degenerative striatal disease necropsy of one case revealing gross necrosis of the globus pallidus (symmetrical) and substantia nigra Arch Neurol and Psychiat 19 5 XIII 549
91 SCHEFTEL Y Pelizaeus Merzbacher disease (familial centro lobar sclerosis) Jour Nerv and Ment Dis 1931 LXXIV 1,5
29 ZIMMERMAN H and YANNET J H Cerebral sequelae of icterus gravis neonatorum Am Jour Dis Child 1933 XLV ,40 and XLIX 418
93 FITZGERALD G M GREENFIELD J G and KOUNINE B Neurological sequelae of Kernicterus Brain 1939 LXII 9
94 KLINGMAN W O and CARLSON E R Cerebral sequelae of severe jaundice in the newborn Bull Neurol Inst New York 193 VI 228
295 HECKER J F C The Epidemics of the Middle Ages Trans by Babington Sydenham Society London 1844
296 DAVIDSON A Choreomania an historical sketch with some account of an epidemic observed in Madagascar Edinburgh Med Jour 1867 XIII 1 4
297 BERNT J Monographia Choreae Sti Viti Prague 1810 cited by See [9]

59 ANTON G Ueber die Betheiligung der grossen basalen Gehirnganglien bei Bewegungstorungen und inbesondere bei Chorea Jahrb f Psychiat u Neurol 1896 XIV 141
260 OPPENHEIM H and VOGT C Nature et localisation de la paralysie pseudo bulbaire congenitale et infantile Jour f Psychol u Neurol 1911 XVIII 93
61 VOGT C Quelques considerations generales a propos du syndrome du corps strie Jour f Psychol u Neurol 1911 XVIII 4,9
6 FREUND C S and VOGT C Un nouveau cas d etat marbre du corps strie Jour f Psychol u Neurol 1911 XVIII 489
63 VOGT C and VOGT O Erster Versuch einer pathologisch anatomischen Einteilung striarer Motilitatsstorungen nebst Bemerkungen uber seine allgemeine wissenschaftliche Bedeutung Jour f Psychol u Neurol 1919 XXIV 1
64 VOGT C and VOGT O Zur psychiatrischen Wurdigung der Antonschen Entdeckung und Wertung des Status marmoratus striati Jour f Psychol u Neurol 1938 XXXVIII 38,
65 BIELSCHOWSKY M Ueber den Status marmoratus des Striatums und atypische Markfasergeflechte der Hirnrinde Jour f Psychol u Neurol 19 4 XXXI 1 5
266 LOWENBERG K and MALAMUD W Status marmoratus etiology and manner of development Arch Neurol and Psychiat 1933 XXIX 104
267 ONARI K Ueber zwei klinisch und anatomisch kompliziertliegende Falle von Status marmoratus Zeitschr f d ges Neurol u Psychiat 19 5 XCVIII 45,
68 SCHOLZ W Zur Kenntnis des Status marmoratus (infantile partielle Striatum sklerose) Zeitschr f d ges Neurol u Psychiat 19 4 LXXXVIII 355
69 MASSALONGO R Dell atetosi doppia Coll ital Letture sulla Medicina V No 3 cited by Audry [3]
270 COLLIER J S Cerebral diplegia Brain 1899 XXII 3,3 and 19 4 XLVII 1
271 NORMAN R M An example of status marmoratus of the cerebral cortex Jour Neurol and Psychopathol 1938 I ,
72 CASE T J Status marmoratus related to early encephalitis Arch Neurol and Psychiat 1934 XXXI 81,
73 SPATZ H Ueber Encephalitis und Encephalitiden Nervenartz 1931 IV 466 and 531 cited by Norman [6]
74 PHELPS W M The management of cerebral palsies Jour Am Med Assoc 1941 CXVII 16 1
275 PHELPS W M Evidences of improvement in cases of athetosis treated by re education Res Publ Assoc Res Nerv and Ment Dis 194 XXI 5 0
276 CARLSON E R Treatment of athetosis by retraining Res Publ Assoc Res Nerv and Ment Dis 194 XXI 534
277 BUCY P C and BUCHANAN D Athetosis Brain 193 LV 4,9
8 BUCY P C and CASE T Athetosis Arch Neurol and Psychiat 1937 XXXVII 983

2 9 BUCY P C Cortical extirpation in the treatment of involuntary movements Res Publ Assoc Nerv and Ment Dis 1942 XXI 551

280 KLEMME R M Surgical treatment of dystonia with report of one hundred cases Res Publ Assoc Nerv and Ment Di 194 XXI 596

81 NAFFZIGER H Discussion of Bucy s paper [78] Arch Neurol and Psychiat 1937 XXXVII 101

8 AMMOSOW M M Zur pathologischen Anatomie der pallidaren Formen von Athetose Jour f Psychol u Neurol 1931 XLI 3 4

83 FISHER O Zur Frage der anatomi chen Grundlage der Athetose double und der po themiplegischen Bewegungstorungen uberhaupt Zeitschr f d ges Neurol u Psychiat 1911 VII 463

84 ROTHMANN M Demonstration zu den Zwangsbewegungen des Kindesalters Zentbl f Neurol 1915 XXXIV 444

85 HALLERVORDEN J and SPATZ H Eigenartige Erkrankung im extrapyrami dalen System mit besonderer Beteiligung des Globus Pallidu und der Sub stantia Nigra Ein Beitrag zu den Beziehungen zwi chen diesen beiden Zen tren Zeitschr f d ges Neurol u Psychiat 19 LXXIX 254

86 KALINOWSKY L Familiare Erkrankung mit besonderer Beteiligung der Stammganglion Monatschr f Psychiat 192, LXVI 168

8 HURST E W On the so called calcification in the basal ganglia of the brain Jour Path and Bact 1926 XXIX 65

88 HELFAND M Status pigmentatus its pathology and its relation to Haller vorden Spatz di ease Jour Nerv and Ment Dis 1935 LXXXI 66

89 OSMAN M and SCHUKRE I Beitrag zur Histopathologie der Hallervorden Spatzschen Erkrankung Deutsch Zeitschr f Nervenheilk 1935 CXXXVI 8

90 WOODS A H and PENDLETON L Fourteen simultaneous cases of an acute degenerative striatal disease necropsy of one case revealing gross necrosis of the globus pallidus (symmetrical) and substantia nigra Arch Neurol and Psychiat 1925 XIII 549

91 SCHEFTEL Y Pelizaeus Merzbacher di ease (familial centro lobar sclero is) Jour Nerv and Ment Dis 1931 LXXIV 1 5

9 ZIMMERMAN H and YANNET J H Cerebral sequelae of icterus gravis neonatorum Am Jour Dis Child 1933 XLV ,40 and XLIX 418

93 FITZGERALD G M GREENFIELD J G and KOUNINE B Neurological equelae of Kernicterus Brain 1939 LXII 29

294 KLINGMAN W O and CARLSON E R Cerebral sequelae of severe jaun dice in the newborn Bull Neurol Inst New York 1934 VI 2 8

95 HECKER J F C The Epidemics of the Middle Ages Trans by Babington Sydenham Society London 1844

296 DAVIDSON A Choreomania an historical sketch with some account of an epidemic observed in Madagascar Edinburgh Med Jour 1867 XIII 1 4

297 BERNT J Monographia Choreae Sti Viti Prague 1810 cited by See [99]
Vol VI 1 15

59 ANTON G Ueber die Betheiligung der grossen basalen Gehirnganglien bei Bewegungstorungen und inbesondere bei Chorea Jahrb f Psychiat u Neurol 1896 XIV 141
60 OPPENHEIM H and VOGT C Nature et localisation de la paralysie pseudo bulbaire congenitale et infantile Jour f Psychol u Neurol 1911 XVIII 93
61 VOGT C Quelques considerations generales a propos du syndrome du corps strie Jour f Psychol u Neurol 1911 XVIII 479
6 FREUND C S and VOGT C Un nouveau cas d etat marbre du corps strie Jour f Psychol u Neurol 1911 XVIII 489
63 VOGT C and VOGT O Erster Versuch einer pathologisch anatomischen Einteilung striarer Motilitatsstorungen nebst Bemerkungen uber seine allgemeine wissenschaftliche Bedeutung Jour f Psychol u Neurol 1919 XXIV 1
64 VOGT C and VOGT O Zur psychiatrischen Wurdigung der Antonschen Entdeckung und Wertung des Status marmoratus striati Jour f Psychol u Neurol 1938 XXXVII 387
65 BIELSCHOWSKY M Ueber den Status marmoratus des Striatums und atypische Markfasergeflechte der Hirnrinde Jour f Psychol u Neurol 19 4 XXXI 1 5
66 LOWENBERG K and MALAMUD W Status marmoratus etiology and manner of development Arch Neurol and Psychiat 1933 XXIX 104
267 ONARI K Ueber zwei klinisch und anatomisch kompliziertliegende Falle von Status marmoratus Zeitschr f d ges Neurol u Psychiat 19 5 XCVIII 457
68 SCHOLZ W Zur Kenntnis des Status marmoratus (infantile partielle Striatum sklerose) Zeitschr f d ges Neurol u Psychiat 19 4 LXXXVIII 355
69 MASSALONGO R Dell atetosi doppia Coll ital Letture sulla Medicina V No 3 cited by Audry [53]
270 COLLIER J S Cerebral diplegia Brain 1899 XXII 373 and 19 4 XLVII 1
271 NORMAN R M An example of status marmoratus of the cerebral cortex Jour Neurol and Psychopathol 1938 I 7
7 CASE T J Status marmoratus related to early encephalitis Arch Neurol and Psychiat 1934 XXXI 817
73 SPATZ H Ueber Encephalitis und Encephalitiden Nervenartz 1931 IV 466 and 531 cited by Norman [6]
274 PHELPS W M The management of cerebral palsies Jour Am Med Assoc 1941 CXVII 16 1
75 PHELPS W M Evidences of improvement in cases of athetosis treated by re education Res Publ Assoc Res Nerv and Ment Dis 194 XXI 5 9
276 CARLSON E R Treatment of athetosis by retraining Res Publ Assoc Res Nerv and Ment Dis 194 XXI 534
77 BUCY P C and BUCHANAN D Athetosis Brain 193 LV 479
78 BUCY P C and CASE T Athetosis Arch Neurol and Psychiat 1937 XXXVII 983

320 HEITTER J A A contribution to the pathology of chronic progressive chorea Brain 1913 XXXV 2 6

321 MARIE P and LHERMITTE J Les lesions de la choree chronique progressive la degeneration atrophique cortico striee Ann med 1914 I 18

322 DUNLAP C B Pathologic changes in Huntington s chorea with special reference to the corpus striatum Arch Neurol and Psychiat 19 XVIII 867

323 ANGLADE Discussion de les chorees chroniques Rev Neurol 1909 XVII 1056

324 HUGHES E M Social significance of Huntington s chorea Am Jour Psychiat 19 5 IV 537

325 MINSKI L and GUTTMANN E Huntington s chorea a study of thirty four cases Jour Ment Sci 1938 LXXXIV 1

326 SMITH H History of a case of Huntington s chorea Med Rec New York 1898 LIV 422

3 ROSANOFF A J and HANDY L M Huntington s Chorea in twins Arch Neurol and Psychiat 1935 XXXIII 839

328 CURRAN D Huntington s chorea without choreiform movements Jour Neurol and Psychopathol 19 0 X 305

329 DIEFENDORF A R Mental symptoms of Huntington s chorea Neurographs 1908 I 1 8

330 NOTKIN J Convulsive manifestations of Huntington s chorea Jour Nerv and Ment Dis 1931 LXXIV 149

331 BOINET E Athetose double hereditaire chronique de l adulte Rev Neurol Paris 1900 VIII 63

33 HOCHHEIMER W Zur Psychologie des Choreatikers Jour f Psychol and Neurol 1936 XLVII 49

333 LION E G and KAHN E Experiential aspects of Huntington s chorea Am Jour Psychiat 1938 XCV 16

334 KLEIST K Untersuchungen zu Kenntnis der psychomotorischen Bewegungstorungen bei Geisteskranken 1908 and 1909 Berlin quoted by Minski and Guttmann

335 SPILLANE J and PHILLIPS R Huntington s chorea in South Wales Quart Jour Med 1937 VI 403

336 KEHRER F Erblichkeit und Nervenleiden Foerster Wilmanns Monogr d ges Neurolog u Psychiat Heft 50 J Springer Berlin 19 8

337 REISCH O Studien an einer Huntington Sippe ein Beitrag zur Symptomatologie verschiedener Studien der Chorea Huntington Arch f Psychiat 19 9 LXXXVI 3 7

338 PATZIG B Vererbung von Bewegungsstorungen Zeitschr f induct Abstammungslehre 1935 LXX 4 6

339 LANNOIS M and Paviot J La nature de la lesion histologique de la choree de Huntington Neurographs 1908 I 105

340 STONE T J and FALSTEIN E I Pathology of Huntington s chorea Jour Nerv and Ment Dis 1938 LXXXVIII 60 and 773

98 DUNGLISON R The Practice of Medicine Vol II p 45 Lea and Blanchard Philadelphia 184
99 SEE G De la Choree Mem Acad nationale med Paris 1850 XV 373
300 LYON I W Chronic hereditary chorea Am Med Times New York 186 VII 89
301 JELLIFFE S E A contribution to the history of Huntington s chorea—a preliminary report Neurographs Vol 1 No p 116 1908
30 HUNTINGTON G On chorea Med and Surg Reptr Philadelphia 1905 XXVI 317
303 DREWRY W F Chronic progressive chorea report of an interesting case in a negro Charlotte Med Jour 1895 VII 318
304 DERCUM F X Adult chorea Internat Clin 1891 III 9
305 TILNEY F A family in which the choreic strain may be traced back to colonial Connecticut Neurographs 1908 I 1 4
306 VESSIE P R On the transmission of Huntington chorea for 300 years—the Bures family group Jour Nerv and Ment Dis 193 LXXVI 553
307 HATTIE W H Huntington s chorea Am Jour Insar 1909 LXVI 1 3
308 CRITCHLEY M Huntington s chorea and East Anglia Jour State Med 1934 XLII 575
309 DAVENPORT C B and MUNCIE E B Huntington s chorea in relation to heredity and eugenics Am Journ Insan 1916 LXXIII 195
310 HAMILTON A S A report of twenty seven cases of chronic progressive chorea Am Jour Insan 1908 LXIV 403
311 HUET E De la Choree chronique Pub Bureaux du Progres Paris 1889
312 ENTRES J L Zur Klinik und Vererbung der Huntingtonschen Chorea Foerster Wilmann s Monogr d ges Neurol u Psychiat Heft 27 III Springer Berlin 1921
313 JOSEPHY H Chorea Huntington in Bumke und Foerster s Handbuch der Neurologie J Springer Berlin 1936 XVI , 9
314 SJOGREN I Vererbungsmedizinische Untersuchungen ueber Huntington s Chorea in einer schwedischen Bauernpopulation Zeitschr f d menschl Vererbungskonstitutionlehre 1935 XIX 135 cited by Minkl and Guttmann[3]
315 BELL J Huntington s chorea The Treasury of Human Inheritance Vol IV Pt 1 Cambridge University Press London 1934
316 SINKLER W On hereditary chorea with a report of three additional cases and details of an autopsy Med Rec New York 1892 XLI 81
317 OSLER W Remarks on the varieties of chronic chorea and a report upon two families of the hereditary form with one autopsy Jour Nerv and Ment Dis 1893 XVIII 97
318 OSLER W On Chorea and Choreiform Affections Blakiston Philadelphia 1894
319 ALZHEIMER A Ueber die anatomische Grundlage der Huntingtonschen Chorea und die choreatischen Bewegungen uberhaupt Zentbl f Neurol 1911 XXX 891

CHAPTER VII

LESIONS OF THE MEDULLA OBLONGATA

By GEORGE RIDDOCH

Revised by J. PURDON MARTIN

TABLE OF CONTENTS

INTRODUCTION

The medulla is concerned in the functions of respiration, circulation, alimentation, articulation and phonation through the nerves which arise from it. These nerves are the glossopharyngeal, vagus, accessorius and hypoglossal. As a portion of the brain stem it is also a conducting pathway for the long tracts passing to and from the spinal cord, and in this part of their course the cerebrospinal and spinocerebral tracts undergo important alterations in position. The pyramidal fibers decussate in the lower part of the medulla (decussation of the pyramids) and just above this level the headward fibers from the posterior column nuclei begin to cross over to the other side (decussation of the fillet). Thirdly, the medulla contains on each side an important nucleus, the olivary body, which has close connections with the cerebellar system; its crinkled outline is a striking feature on any cross section of this part of the brain stem. The bulb is so small and its structure so complex and important that lesions even of small size often lead to disastrous results.

This section will be devoted to the consideration of those disorders only which follow primary disease of the medulla. General diseases of the nervous system, such as disseminated sclerosis, cerebrospinal syphilis, acute polioencephalomyelitis, encephalitis lethargica and botulism, in

341 LANNOIS M Classification des chorees arythmiques Rev Neurol 1895 III 66
342 ALCOCK N S A note on the pathology of senile chorea (non hereditary) Brain 1936 LIX 376
343 DAVISON C GOODHART S P and SHLIONSKY H Chronic progressive chorea the pathogenesis and mechanism a histopathologic study Arch Neurol and Psychiat 1932 XXVII 906
344 BRISSAUD E La choree variable des degeneres Rev Neurol 1896 IV 417
345 LEWIS A and MINSKI L Chorea and psychosis Lancet 1935 I 536
346 MOUNT L A and REBACK L S Familial paroxysmal choreoathetosis Arch Neurol and Psychiat 1940 XLIV 841
347 DAVISON C Spastic pseudo sclerosis (cortico pallido spinal degeneration) Brain 1932 LV 47
348 CRITCHLEY M and GREENFIELD J G Jakob s syndrome (senile dementia with parkinsonism) Proc Royal Soc Med Lond 1937 XXX 1100

December 1 1945

comes impossible the voice is nasal and fluids regurgitate through the nose With implication of the pharynx swallowing which is already much impeded by weakness of the tongue becomes increasingly difficult Semisolids are swallowed better than liquids

With paralysis of the vocal cords the patient s misery is almost complete Inarticulate almost voiceless swallowing with difficulty while saliva pours from his open lips he presents a picture of great distress Respiration is weak and labored the pulse rapid feeble and irregular anginal attacks are not infrequent and syncope may prove fatal

Wasting of the affected muscles especially of the tongue progresses steadily with lo s of power but a response to faradic stimulation is obtained so long as there are any active mu cle fibers left Sensibility is not impaired The palatal and pharyngeal reflexes at first are diminished and later abolished In simple bulbar paralysis the trunk and limbs are not affected but before long the underlying pathological process involves the pyramidal tracts and corresponding alterations in the superficial and deep reflexes appear

The course of the disease always is progressive and terminates usually in one to four years Gradual weakness from inanition bronchitis broncho pneumonia respiratory and cardiac failure are the most frequent causes of death

Pathology — The nervous and muscular changes are analogous to those found in amyotrophic lateral sclerosis There is a slow degeneration of the cells of the bulbar motor nuclei the morbid condition being revealed only by micros opic examination The cells waste and lose their processes and the axis cylinders degenerate The interstitial tissue increases in amount and contains granule corpuscles Spider cells usually are present The anterior p ramids often are involved in the degenerative process but to a less extent than the cellular elements Both sides of the medulla are affected fairly uniformly and the most advanced changes are found almost constantly in the cells of the hypoglossal nuclei

Treatment — The physician unfortunately is powerless at present to arrest the progress of the disease The most that can be done is to attend to the nutrition of the patient to endeavor to make his existence as comfortable as possible and to guard against serious complications Care should be taken that he is never left alone at meal times since by his own efforts u ually he is unable to expel particles of food which may have dropped into his larynx Semisolid pulpy foods such as meat or fish pounded into a thick paste are swallowed better than liquids or solids In the later stages artificial feeding by means of a soft catheter passed through the nose or mouth is necessary

which the medulla may happen to be implicated and the effects of compression or invasion by tumors growing from the pons cerebellum or base of the skull are dealt with in other sections

Primary new growths and abscess formation are rare and gross traumatic injury as from penetrating wounds and fracture dislocation of the atlas and axis result as a rule in immediate death from respiratory paralysis Severe hemorrhage into the medulla or fourth ventricle usually proves fatal either immediately or within a few hours death being preceded by coma stertorous breathing and sometimes convulsions In the vast majority of cases of bulbar palsy in which life is preserved for some time the lesion is produced either by softening of the tissues from thrombotic or embolic occlusion of a branch of the vertebral anterior spinal or posterior cerebellar arteries which supply the medulla or by inflammatory or degenerative changes in the nerve nuclei

Chronic Bulbar Paralysis

Synonyms — Labioglossopharyngeal paralysis (Duchenne 1860) progressive bulbar paralysis (Wachsmuth 1864) polioencephalitis inferior chronica (Wernicke)

The pathological basis of this disorder is a bilateral degeneration of the cranial nerve nuclei of the bulb and the disease is the medullary counterpart of amyotrophic lateral sclerosis with which frequently it is associated It is the commonest form of bulbar palsy A few cases have been recorded in the second and third decades of life but its incidence falls most heavily in middle age Males are attacked more often than females rarely several members of a family have been affected For the most part no cause immediate or remote can be traced

Symptoms — Articulation is as a rule disturbed first difficulty being experienced in the pronunciation of those consonants for the production of which precise movements of the tongue are necessary Thus l r n t d th and s are pronounced indistinctly and the defect at first is most apparent when the patient is tired The disease evolves slowly but soon the tongue begins to waste and shows longitudinal furrows and fibrillary twitchings The patient has difficulty in protruding the tongue tip beyond his teeth and in moving it into the cheeks or towards the palate

As a rule the orbicularis oris is involved after the tongue and the patient is unable to purse his lips whistle and articulate explosive labials such as p and b and to emit the vowels o and u The lower lip begins to droop and saliva to dribble from the open mouth The paralytic process extends to the soft palate and pronunciation of the gutturals k and g be

part of the descending trigeminal nucleus (4) impairment of pain and temperature on the trunk and limbs of the opposite side owing to the lesion of the spino thalamic tract in some cases similar impairment is found on the opposite side of the face because of the involvement of the fibres which have crossed from the descending trigeminal nucleus of that side to join the spino thalamic tract of the affected side (5) light pto is a small pupil and possibly slight exophthalmos on the affected side owing to involvement in the lesion of the fibres of the sympathetic system descending through the medulla

A good deal of recovery usually occurs but the patient may be left with some troublesome pains or parasthesiæ

Lesions of Other Arteries to the Medulla

Lesions of the other arteries supplying the medulla are less common but thrombosis of one of the more medial branches may give rise to a crossed syndrome in which there is hemi paralysis and later hemi atrophy of the tongue from involvement of the emerging fibres of the hypoglossal nerve and paralysis of the limbs on the opposite side of the body from infarction of the pyramid

Lesions of the medulla may be associated also with incoordination of the limbs on the same side from interruption of cerebellar paths and cardio respiratory disturbances of serious nature are not uncommon Although albuminuria and glycosuria have been observed with lesions of the floor of the fourth ventricle they are not frequent symptoms of acute bulbar paralysis

Diagnosis of Bulbar Paralysis

The diagnosis of bulbar paralysis often is difficult especially if a complete history of the onset and evolution of the complaint is not obtained Myasthenia gravis which is a commoner disease than chronic bulbar paralysis frequently involves the same muscular structures It may be distinguished by the variability of the paralysis its liability to affect the external ocular muscles as chronic bulbar paralysis never does the absence of signs of involvement of the pyramidal tracts and the temporary recovery of the paralysis under the influence of prostigmin

The so-called pseudobulbar palsies resulting from supranuclear lesions can be differentiated from the disorders which follow nuclear or infranuclear disease by the absence of wasting fibrillary contractions and electrical changes in the muscles by preservation of the palatal and

Fatigue not only of the weak muscles but also of the body in general must be avoided The patient must be kept warmly clad and protected from exposure to the risks of nasal catarrh and bronchitis

Strychnin arsenic quinin and other so called nerve tonics are often prescribed and vitamin preparations and liver and other tissue extracts have been extensively tried also but that beneficial results follow their administration is problematical Treatment by electrical stimulation is not encouraging

Acute (Apoplectiform) Bulbar Paralysis

This form of bulbar palsy is vascular in origin and usually is the result of thrombosis or embolism of one or more branches of the basilar artery and especially of the posterior inferior cerebellar arteries It is a disorder of middle and old age but examples are met with occasionally in young people The onset always is sudden with giddiness and vomiting consciousness may be lost and convulsions sometimes occur The disturbance of function is greatest at the beginning and if the patient survives the early stage recovery takes place to some extent usually within a few days leaving a chronic non progressive malady

Thrombosis of the Posterior Inferior Cerebellar Artery

The posterior inferior cerebellar artery supplies the lower half of the corresponding cerebellar hemisphere and the inferior cerebellar peduncle (corpus restiforme) but it supplies also the lateral portion of the medulla dorsal to the olivary body This portion includes the various nuclei connected with the glosso pharyngeal vagus and accessory (9th 10th and 11th) nerves the substantia Rolandi in which lies the descending nucleus of the trigeminal (5th) nerve and the spino thalamic tract which is passing up just posterior to the olive and conveys painful and thermal stimuli from the opposite side of the body Thrombosis of the artery causes a sudden onset of intense vertigo which throws the patient to the ground and causes him to vomit when he recovers sufficiently he finds that he has difficulty in swallowing and his voice is somewhat nasal and husky More detailed examination shows (1) signs of a cerebellar lesion on one side viz nystagmus maximal to the side of the lesion ataxia and some hypotonia in the limbs of the same side (2) unilateral paralysis of the palate pharynx and larynx consequent on the lesion of the nucleus ambiguous of the vagus (3) loss of appreciation of pain and temperature on a portion of the face on the same side due to the involvement of

CHAPTER XIII

DISFASFS OF THE CEREBRAL MENINGES

By H CAMPBELL THOMSON

Table of Content

The Meninges

The meninges form the covering membranes of the brain and spinal cord They con ist of three layers known a dura mater arachnoid and pia mater re pectively

Dura Mater —The outermost of these coverings i the dura mater which

pharyngeal reflexes and of the involuntary movements of yawning laughing and coughing The symptoms as a rule develop first on one side and then usually after a considerable interval on the other

With nuclear and infranuclear lesions the affected muscles waste and give altered electrical reactions palatal and pharyngeal reflexes are diminished or lost and fibrillary twitchings in the muscles often are present

Cases of acute bulbar palsy develop rapidly and remote symptoms in the trunk and limbs almost invariably are present Chronic bulbar paralysis is to be distinguished from the pressure symptoms of a slow growing extramedullary tumor by the bilateral and usually symmetrical nature of the disorder

Lesions of the Olivary Body

Recent observations indicate that lesions of the olivary body or of a band of fibres passing down to it from the red nucleus give rise to myoclonic movements of the soft palate nystagmus of the palate and in some cases these jerking movements affect also the larynx tongue lips and eyes This symptom usually is the result of a vascular lesion but may arise in the course of disseminated sclerosis and other diseases

BIBLIOGRAPHY

1 HEAD H and HOLMES G Brain Lond 1911 XXXIV 102
2 TURNER W A Brain Lond 1895 XVIII 231
3 GUILLAIN G Proceedings of the Royal Society of Medicine London 1938 XXXI 1031

Sept 1 1939

fluid is largely protective in character by forming a cushion which neutralizes the effects of vibrations and shocks which would otherwise be transmitted to the brain and spinal cord. Various other functions of a chemical nature have also been suggested but about these there is up to the present no certainty. The fluid apparently circulates from the ventricles to the subarachnoid space and from there passes down the cord. One of its characteristics which has an important bearing on treatment of nervous diseases is the difficulty which substances have in passing into it from the blood.

Normal cerebrospinal fluid is a clear water like fluid with no sediment and has a specific gravity varying between 1.001 and 1.008. Besides water which forms about ninety nine per cent of its composition and a small quantity of solids consisting of proteids, extractives and salts, there is a substance which reduces Fehling's solution and which is now known to be glucose. The value of the cerebrospinal fluid for diagnostic purposes is great. In abnormal states there may be alterations in its appearance and constituents both microscopical and bacteriological. In many instances of meningitis the fluid besides flowing under an increased pressure becomes turbid and in addition to bacteriological evidence of disease shows on microscopical examination the presence of lymphocytes and other cellular changes. In addition to its diagnostic value the withdrawal of fluid for therapeutic purposes and consequent relief of pressure is often followed by substantial relief.

Lumbar Puncture

The cerebrospinal fluid is obtained by lumbar puncture which is accomplished by passing a needle through the spinal membranes in the interval between the third and fourth or the fourth and fifth lumbar vertebrae. The

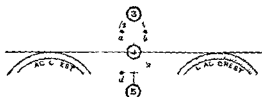


Fig. 1.—Diagram showing positions [illegible] for lumbar puncture. (*H. [illegible]*) (From [illegible] *Diseases of the Nervous System*)

guide to these spots (Fig. 1) is a line drawn between the highest points of the iliac crests, which line passes through the spinous process of the fourth lumbar vertebra, so that the puncture should be made in the interspinous interval just above or below this line, either in the middle line or, as some recommend, slightly (rather less than half an inch) to one side of it. The

in the skull consists of two layers the outer being attached to the inner surface of the cranial bones while the inner layer forms the outer wall of the subdural space In some parts the two layers are separated to form blood sinuses of which the superior longitudinal sinus is an example Prolongations of the dura mater the chief of which are the falx cerebri falx cerebelli and tentorium cerebelli act as supports to the different parts of the brain In the spinal canal the inner layer only of the dura mater can be recognized The blood supply of the dura mater is obtained from the meningeal arteries and its nerve supply chiefly from the trigeminal nerves

Arachnoid —The arachnoid is a delicate membrane situated between the dura mater and the pia mater While its outer surface is in close apposition with the dura mater the two surfaces being separated merely by a little cerebrospinal fluid which enables them to glide freely over each other its inner surface is in contact with the pia mater only in parts for while the pia mater closely follows the irregularities of the brain surface and dips down into all the hollows the arachnoid lies loosely over them and where the hollows are deep as they are for instance at the base of the brain the space between the arachnoid and the pia are of considerable dimensions The interval between these two membranes is known as the subarachnoid space It is occupied by cerebrospinal fluid and the larger spaces are known as subarachnoid cisternae

The *pia mater* is a thin vascular membrane which closely invests the surface of the brain dipping into all the grooves and also sending out prolongations known as the velum interpositum which in the ventricle form the choroid plexuses The roof of the fourth ventricle consists chiefly of one of these prolongations and in it there is an aperture known as the foramen of Magendie this and two other apertures into the fourth ventricle form the principal channels by which the circulation of cerebrospinal fluid takes place between the subarachnoid space and the ventricles

The arachnoid and the pia mater together are known as the leptomeninges and any inflammatory process of them is denoted by the term leptomeningitis

The Cerebrospinal Fluid

The cerebrospinal fluid occupies the space between the arachnoid and pia mater *i e* the subarachnoid space The views as to the origin of this fluid are not unanimous, for while it seems clear that the choroid plexus is the active agent in its production it is uncertain whether the fluid is produced by a process of secretion or by one in which the constituents are separated from the blood by a process of filtration The function of the

fluid is largely protective in character by forming a cushion which neutralizes the effects of vibrations and shocks which would otherwise be transmitted to the brain and spinal cord. Various other functions of a chemical nature have also been suggested but about these there is up to the present no certainty. The fluid apparently circulates from the ventricles to the subarachnoid space and from there passes down the cord. One of its characteristics which has an important bearing on treatment of nervous diseases is the difficulty which substances have in passing into it from the blood.

Normal cerebrospinal fluid is a clear water-like fluid with no sediment and has a specific gravity varying between 1.001 and 1.008. Besides water which forms about ninety-nine per cent. of its composition and a small quantity of solid consisting of proteids, extractives and salts, there is a substance which reduces Fehling's solution and which is now known to be glucose. The value of the cerebrospinal fluid for diagnostic purposes is great. In abnormal states there may be alterations in its appearance and constituents both microscopical and bacteriological. In many instances of meningitis the fluid besides flowing under an increased pressure becomes turbid and in addition to bacteriological evidence of disease shows on microscopical examination the presence of lymphocytosis and other cellular changes. In addition to its diagnostic value the withdrawal of fluid for therapeutic purposes and consequent relief of pressure is often followed by substantial relief.

Lumbar Puncture

The cerebrospinal fluid is obtained by lumbar puncture which is accomplished by passing a needle through the spinal membranes in the interval between the third and fourth or the fourth and fifth lumbar vertebrae. The

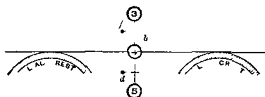


Fig. 1.—Diagram showing position suitable for lumbar puncture. (*H. MacCormac.*)
(From Campbell Thomson, *Diseases of the Nervous System.*)

guide to these spots (Fig. 1) is a line drawn between the highest points of the iliac crests, which line passes through the spinous process of the fourth lumbar vertebra, so that the puncture should be made in the interspinous interval just above or below this line, either in the middle line or, as some recommend, slightly (rather less than half an inch) to one side of it. The

strictest aseptic precautions should be taken to avoid infection. If the pressure is normal the fluid flows out drop by drop, but where the pressure is increased, as it is in many cases of meningitis, the flow is more forcible. Occasionally a little blood from some small vessel is mixed with the first few drops but this usually soon disappears. The patient should be in the recumbent position with the knees drawn well up and the head and shoulders bent forward so that the trunk is thereby rendered convex backwards, and when all is ready a stout needle fitted with a stylet is inserted directly forwards and, if outside the middle line, a little inwards as well. If bone is struck, the needle should be withdrawn a little and slightly altered in direction. The ligamentum subflavum may also cause some slight resistance, but it can usually be distinguished from that of bone. After the first few drops have been allowed to pass and the fluid is seen to be clear of blood, it should be collected in a sterile test tube.

If there is no increase of pressure about 5 to 10 c.c. only should be withdrawn, but more can be taken if the pressure is increased and in some cases of meningitis where the amount of fluid is excessive as much as 15 c.c. to 40 c.c. may be removed, the condition of the pulse always being carefully watched to indicate any sign of shock which should at once be a signal to stop.

Cerebral Meningitis

Cerebral meningitis, *i.e.*, inflammation of the membranes of the brain, may occur as part of a general infective disorder or it may result from extension of local disease of the bones of the skull, as for example middle ear disease or direct injury to the cranium.

Classification of the different forms may be based upon anatomical considerations or upon the varieties of the microorganisms which are the infective agents. According to the first of these methods we can recognize (1) pachymeningitis externa and interna, in which the dura mater is inflamed, and (2) leptomeningitis, in which the pia mater and arachnoid are diseased, *though clinically it naturally often happens that all the membranes are* affected together in such a manner that no definite anatomical distinction can be made.

In pachymeningitis externa the outer aspect of the dura mater is first diseased, the trouble usually arising from extension from disease of the neighboring bones or sinuses such as from mastoid disease or injuries to the bones of the skull. The membrane becomes thickened, inflamed and adherent to surrounding structures, the inflammation remaining localized or spreading according to the intensity and nature of the infection.

Pachymeningitis interna is usually associated with chronic degenerative

diseases such as general paralysis senile dementia and chronic alcoholism The membrane becomes thickened and the inflammation spreading to the arachnoid and pia mater causes adhesions to form with the brain tissue beneath The condition is probably due to the occurrence of slow subdural venous hemorrhages which form hematomata from which this variety has also received the name of pachymeningitis hemorrhagica

Leptomeningitis in which there is inflammation of both pia and arachnoid membranes may be either acute or chronic and may arise from infection of microorganisms of local or general origin

Meningitis may be otherwise classified according to the type of infection and among the principal infecting microorganisms are the meningococcus of cerebrospinal fever tubercle bacillus spirochaeta pallida pneumococcus streptococcus and staphylococcus and thus one speaks of cerebrospinal meningitis tuberculous meningitis syphilitic meningitis and so on according to the nature of the infection

The symptoms of meningitis differ according to the general or localized character of the inflammation and the rapidity with which it runs its course and clinically the cases may often conveniently be spoken of as acute or chronic general meningitis and localized meningitis such as for instance is often seen as a result of syphilis

Injuries to the Meninges

Injuries to the meninges may result from violence to the head of any description Among the common causes are injuries at childbirth and in later life blows on the head

One of the most serious results of such an injury is hemorrhage from one of the branches of the middle meningeal artery The immediate effects of such a blow of this kind may not appear to be serious but after a brief interval the rise of intracranial pressure from the hemorrhage begins to be felt The patient loses consciousness shows signs of progressive hemiplegia with or without convulsions and soon sinks into a deep coma and dies unless the skull can be opened and the bleeding quickly arrested

Experience with war injuries has shown that damage to the membranes and to the cortex underneath may occur from high velocity missiles merely grazing the bones Wilfred Trotter (Brain Lond 1919 XLII 353) has investigated this matter and concludes that the resilience of the skull is such that whenever a missile travelling at high velocity touches the bone the latter is driven in upon the brain with force enough to inflict a considerable bruise and that in such circumstances a contusion of the brain is likely to remain longer than it would in other organs owing to the unyielding char

acter of the cranium which prevents compensatory swelling by which the circulation is maintained through any other bruised organ (See also Trotter Vol VI Chap V) Among the principal symptoms complained of in such cases are headaches and giddiness the former being often brought on by some physical effort as stooping On operation the arachnoid is found to be opaque and distended by a local accumulation of fluid beneath it the condition in some cases amounting to a definite meningitis serosa circumscripta while the brain is discolored from old extravasated blood Trotter finds that the headache can be greatly relieved or completely cured by free removal of bone and incision of the dura over the seat of injury and recommends that the opening in the skull should be closed again some months later

TUBERCULOUS MENINGITIS

Tuberculous meningitis is most often seen in children between two and ten years of age but its occurrence is by no means rare in adults especially as a terminal phase of chronic tubercle elsewhere Indeed in almost every case whether in child or adult an examination after death reveals the presence of tubercles in other organs

Symptoms

The early symptoms are very variable so that the condition may be difficult to recognize in its first stages There are often signs of general disturbance of health due to toxic effects of the tubercles in the meninges or elsewhere for a considerable time before any symptoms indicate localized cerebral trouble Thus the child may be irritable languid and altogether unwell, and if the temperature is taken it will generally be found to be irregular and often a little above normal Vomiting often associated with constipation is frequently an early symptom and if present with other indefinite symptoms as described above should always give rise to suspicion Among the more definite signs that may usher in the disease are severe headache strabismus and perhaps a general convulsion but in most cases the history shows the child to have been unwell for some little time previously

The tubercles in the form of gray semitranslucent granules about the size of a pin s head are situated in the pia mater and are for the most part distributed over the base of the brain In doubtful cases they should especially be looked for between the opercula of the Sylvian fissure and along the course of the middle cerebral artery As a rule they do not spread to any great extent over the cortex of the cerebral hemispheres

It will thus be seen that the symptoms are chiefly produced by (1) irritation and compression of various structures more particularly the cranial nerves at the base of the brain and (2) general rise of intracranial pressure due to the exudation of fluid the free circulation of which is further often limited by the blocking of the foramen of Majendie by adhesions

Attempts have been made to divide the clinical course of the disease into stages according to the predominance of signs of irritation or compression but these so often occur in different relationships of time that any classification on such a basis is bound to be misleading in practice

The Cranial Nerves

These as already stated are very liable to be affected since the tubercles are generally most plentiful at the base of the brain

Olfactory Nerve—This usually does not show any impairment of function

Optic Nerve—Optic neuritis is frequent and when present in a suspected case will at any rate indicate the presence of increased intracranial pressure As the retina is being examined careful search should also be made for tubercles in the choroid which if found to be present will do much to decide the diagnosis

The Oculomotor Nerves (Third Fourth and Sixth)—Affection of one or more of these nerves will give rise to squints ptosis or changes in the pupil all of which are frequently found in this disease Nystagmus may occasionally be seen

Trigeminal Nerve—Signs of impairment of this nerve are not common but if present will be shown by pain over the area of its sensory distribution and of spasm or weakness of the muscles of mastication supplied by its motor branches

Facial Nerve—Irritation of this nerve is shown by twitching of muscles or weakness may result from its paralysis

Auditory Nerve—Deafness to some extent may be present

Glossopharyngeal Nerve—There are usually no symptoms to be found connected with this nerve

Vagus—Irritation of the vagus is no doubt largely responsible for the bradycardia which is often a feature at certain stages of the illness but cardiac irregularities together with alterations in the rhythm of respiration are probably also caused by the general rise of intracranial pressure

Spinal Accessory Nerve—Irritation of the spinal portion of this nerve is probably contributory together with overaction of the cerebellum in causing retraction of the head Retraction of the head is however a much less

acter of the cranium which prevents compensatory swelling by which the circulation is maintained through any other bruised organ (See also Trotter Vol VI Chap V) Among the principal symptoms complained of in such cases are headaches and giddiness the former being often brought on by some physical effort as stooping On operation the arachnoid is found to be opaque and distended by a local accumulation of fluid beneath it the condition in some cases amounting to a definite meningitis sero a circum scripta while the brain is discolored from old extravasated blood Trotter finds that the headache can be greatly relieved or completely cured by free removal of bone and incision of the dura over the seat of injury and recommends that the opening in the skull should be closed again some months later

Tuberculous Meningitis

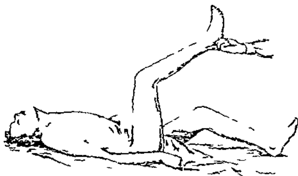
Tuberculous meningitis is most often seen in children between two and ten years of age but its occurrence is by no means rare in adults especially as a terminal phase of chronic tubercle elsewhere Indeed in almost every case whether in child or adult an examination after death reveals the presence of tubercles in other organs

Symptoms

The early symptoms are very variable so that the condition may be difficult to recognize in its first stages There are often signs of general disturbance of health due to toxic effects of the tubercles in the meninges or elsewhere for a considerable time before any symptoms indicate localized cerebral trouble Thus the child may be irritable languid and altogether unwell and if the temperature is taken it will generally be found to be irregular and often a little above normal Vomiting often associated with constipation is frequently an early symptom and if present with other indefinite symptoms as described above should always give rise to suspicion Among the more definite signs that may usher in the disease are severe headache strabismus and perhaps a general convulsion but in most cases the history shows the child to have been unwell for some little time previously

The tubercles in the form of gray semitranslucent granules about the size of a pin s head are situated in the pia mater and are for the most part distributed over the base of the brain In doubtful cases they should especially be looked for between the opercula of the Sylvian fissure and along the course of the middle cerebral artery As a rule they do not spread to any great extent over the cortex of the cerebral hemispheres

variable In some cases signs of local cerebral lesion are a prominent feature from the first while in others the illness may run its course with symptoms so vague as to make the diagnosis uncertain even to the end As a general rule it may be said that the disease begins insidiously with symptoms of lassitude irritability headache and digestive disturbance followed sooner or later by the occurrence of a squint and vomiting As the intracranial pressure rises the mental symptoms become more pronounced irritability and restlessness tend to pass into drowsiness and coma the child lies curled upon one side shunning the light with closed eyes passing excreta unconsciously and occasionally groaning or uttering a shriek known



Fi —Method of obtaining Kernig's sign (After a photograph by D H Th) (From Campbell Thomson D of the Nerv Sys m)

as the hydrocephalic cry The pulse is quick the breathing rapid and irregular in rhythm and the temperature raised Finally the coma deepens the pupils become dilated mucus collects on the corneae the child ceases to swallow any food and the temperature which has been irregular often rises to a considerable height before death takes place

Diagnosis

There is frequently considerable difficulty in arriving at a correct diagnosis during the early stages of the disease especially in children In some cases the symptoms are so ill-defined that it is not possible to estimate their significance until some more definite sign such as strabismus alterations in reflexes or Kernig's sign develops In other instances the onset is more acute and the difficulty will then be to differentiate the condition from that which may accompany a specific fever in its early stages Often a definite decision has to be withheld for a time and there are few cases that

frequent symptom in tuberculous meningitis than in the posterior basic and epidemic cerebrospinal forms

The *hypoglossal nerve* does not usually show any signs of disease

Disturbances in Other Parts of the Brain

Having examined the cranial nerves signs of disordered movements due to disease of the other parts of the brain may be looked for The functions of the pyramidal tracts should be examined by testing the power of the limbs and the state of the reflexes Rigidity of the limbs usually combined with some loss of voluntary power of monoplegic hemiplegic or diplegic distribution may be found according to the localization of the lesions in the region of the motor cortex or elsewhere in the motor tracts Additional signs of cortical disease either from the local deposit of tubercle or consequent on general rise of pressure may be shown by the occurrence of convulsions

The tendon reflexes of arms and legs at this stage will usually be increased and an extensor response of the plantar reflexes giving further indication of an alteration in the functions of the pyramidal tracts will often be found

The abdomen is retracted and is known from its appearance as the scaphoid abdomen The superficial abdominal reflexes are frequently diminished or absent

As already mentioned general rigidity of the trunk and limbs is frequently present and associated with this rigidity is the phenomenon known as Kernig s sign which is an indication of cerebral irritation and is said to be present in over eighty per cent of cases of meningitis This sign depends upon increased tone (hypertonus) of muscles and is obtained by flexing one leg at the knee and hip the patient meanwhile lying flat on the back the other leg being kept extended (Fig 2) If the tone of the muscles is increased the degree of extension which can be obtained at the knee joint while the thigh is flexed on the abdomen is considerably less than normal owing to resistance of the hamstring muscles

The irritability of the vasomotor system is increased and a slight stroking of the skin with a hard object is quickly followed by a wheal a sign which is known as the tache cérébrale

The pulse during some stages of the disease may be abnormally slow due presumably to stimulation of the vagus but towards the end it generally becomes rapid and irregular The respiratory system also shows signs of irregularity in its action The breathing is generally rapid altered in rhythm often being marked by pauses tending to resemble the form known as Cheyne Stokes respiration

It need hardly be stated that all the signs described above are very

Treatment

So far as any direct benefit is concerned the treatment of tuberculous meningitis is unsatisfactory and no drugs seem to have any effect on the course of the disease Hexamethylenamin may be given for its supposed antiseptic effect on the cerebrospinal fluid Since many of the symptoms are due to the excessive exudation of fluid some temporary improvement may sometimes be obtained by lumbar puncture and consequent relief of pressure but unfortunately in many cases adhesion at the base of the brain prevent the fluid being drawn off with sufficient freedom to give much relief The general symptoms may be relieved to some extent by keeping the patient in a darkened room applying an ice bag to the head and giving such drugs as phenacetin aspirin and salicylates to relieve the headaches Mercury by inunction has been recommended but it is doubtful if it has any value Potassium iodid appears to be useless but should be given if there is any diagnostic doubt of the symptoms being of syphilitic origin Symptoms connected with the heart general circulation or alimentary canal must be treated as required

CEREBROSPINAL MENINGITIS (SPOTTED FEVER)

This disease (see also Herrick Vol V) which is due to infection by a microorganism known as the meningococcus occurs both in epidemic and sporadic form the latter being known clinically as posterior basic meningitis

Etiology

The microorganism is the diplococcus intracellularis of Weichselbaum commonly known as the meningococcus which is a disc shaped Gram negative coccus resembling the gonococcus but distinguishable from it and from the other members of the group by its cultural characteristics

Epidemics tend to occur most often in the winter and spring months but the exact conditions which cause the disease to assume an epidemic form are not known though the sporadic cases no doubt often form the groundwork from which in favorable circumstances an epidemic may arise Atmospheric changes overcrowding chronic catarrhal states and other debilitating influences are probably the factors of most importance in modifying the virulence of the microorganism and the disease spreads most in overcrowded districts One of the most important factors in the dissemination of the disease is the existence of carriers who acquire the

give rise to greater anxiety than that of a child whose symptoms are vaguely suggestive of the onset of tuberculous meningitis the outlook of which is so hopeless General debility with gastrointestinal disturbance and general nervous irritability such as often accompany an attack of influenza or some other infective process in a child may be suggestive of meningitis for a time Where a careful examination shows no positive sign of meningitis one can only form a temporary opinion in the absence of more definite symptoms and await further developments

Meningeal irritation from any other cause, e g consequent on mastoid or middle ear disease may be mistaken for tuberculous meningitis as also may the delirium of pneumonia and bronchopneumonia especially in cases where the cerebral symptoms predominate over those of the chest

In the early stages the symptoms may be ascribed to teething indigestion intestinal worms and other illnesses of childhood, that are accompanied by irritability and general malaise The symptoms of typhoid fever may sometimes for a time be difficult to distinguish from those of tuberculous meningitis but distention of the abdomen enlarged spleen, type of pyrexia and Widal reaction will usually serve to differentiate the two diseases

When the diagnosis of meningitis has been made the tuberculous form has still to be distinguished from the other varieties of which suppurative posterior basic and epidemic cerebrospinal are the chief These three all begin more acutely than the tuberculous form and the suppurative type causes death within a few days Retraction of the head is far more characteristic of the posterior basic and epidemic cerebrospinal varieties Examination of the cerebrospinal fluid generally clears up the diagnosis in doubtful cases

Lumbar puncture in the case of tuberculous meningitis usually yields a clear or only slightly flaky fluid Lymphocytosis is generally present and in a considerable number of cases a microscopical examination may show the presence of tubercle bacilli Usually inoculation of the sediment into a guinea pig produces tuberculosis and gives a positive diagnosis

Prognosis

Cases have occasionally been recorded where patients have recovered from meningeal symptoms which appeared to be due to undoubted tuberculosis but such instances are so extremely rare that for practical purposes the disease must be regarded as one which always causes death The duration of the illness is usually about three weeks from the time of the first appearance of definite symptoms In a large number of cases the meningeal infection is only the terminal stage of a more generalized tuberculosis

The presence of inflammation of the meninges both of the brain and cord is shown by the occurrence of such various symptoms as optic neuritis inequality and fixation of pupil strabismus ptosis facial palsy and deafness by rigidity of the neck and muscles of the body causing retraction of the head and opisthotonos while among the more generalized signs of the nervous disturbance are convulsions delirium coma variations in the rhythms of respiration and heart beat with possibly some localized paralyses of limb such as hemiplegia or paraplegia and other symptoms of nerve irritation such as have already been described in the account of tuberculous meningitis

Inflammation of the different structures of the eyes causing conjunctivitis corneitis iritis may take place and in some cases the destruction may be sufficiently extensive to cause permanent loss of sight Inflammations of the ears nose and lungs are also frequent and bronchopneumonia may be one of the serious complications Herpes round the mouth and a more generalized skin eruption in which there are small hemorrhages are common and it is from the appearance of this latter that the name of "spotted fever" has arisen The pulse and temperature are variable the latter often becoming of the intermittent type Swellings of joints may also take place

It will be seen how widespread the effects are and that there is scarcely any system which may not be affected in an acute case In the fulminating cases the end may come within twenty four hours while in ordinary acute cases of fatal termination death is likely to occur within two or three weeks When the illness takes a favorable turn recovery takes place slowly and from time to time may be interrupted by a return of symptoms which again makes the outlook uncertain Sometimes the acute symptoms give way to those of a more chronic nature in which progressive emaciation and weakness are prominent features and recovery—if it takes place—is then liable to be accompanied by impairment of the mental faculties and hydrocephalus Such cases may last for some weeks during which the patient remains drowsy or semicomatose with incontinence of urine and feces and becomes reduced to a mere skeleton before death occurs from exhaustion or the results of intracranial pressure

Diagnosis

In the early stages the symptoms have to be differentiated from those of other acute infectious diseases and when the presence of meningeal symptoms has become definitely established the cerebrospinal meningitis has further to be distinguished from meningitis due to other forms of infection such as the tubercle bacillus pneumococcus and streptococcus

The characters of the cerebrospinal fluid are often decisive factors in the

meningococcus during an epidemic and retain it in the nasopharynx for quite a long time—it may be for some weeks—without themselves showing any signs of the disease. Such 'carriers' disseminate the infection by coughing and sneezing, and in surroundings which tend to increase the virulence of the meningococcus or lower the resistance of the recipients the disease is undoubtedly widely spread in this manner. Generalized infection probably takes place from the nasopharynx through the blood stream and then becomes mainly localized in the meninges. Outside the body the organism does not possess much vitality, but as it can be found in discharges from the nose as well as in the sputum of patients great care should be taken to prevent the infection from spreading from these sources. Infection of the sinuses is also a common complication. The diplococcus is not very easy to cultivate and grows best on serum agar.

Morbid Anatomy

In the very acute cases there may be little to see with the naked eye beyond congestion of vessels and some excess of serous fluid, but in those of longer duration the exudation is purulent and situated principally at the base of the brain. In the more chronic cases the membranes become thickened and adherent to each other and to the brain substance beneath. The ventricles are distended and contain turbid fluid. Patches of softening may occur in the surface of the brain and the inflammatory process may also extend along the course of cranial and spinal nerves.

Symptoms

The incubation period appears to range between one and five days. The symptoms differ considerably according to the clinical type which the disease shows in any particular individual. In some instances the patient is taken suddenly ill with intense headache and fever, rapidly becomes comatose and dies in a few hours, while on the other hand there are mild cases, the nature of which would probably not be suspected if the presence of an epidemic did not cause particular attention to be paid to them. Between these extremes there are the more ordinary or acute types, in which the onset is characterized by headache, rapid rise of temperature, shivering and perhaps vomiting, with a general feeling of illness such as occurs at the beginning of most acute infectious diseases. The vomiting and pains may both become very troublesome, the latter often being felt in the limbs and other parts of the body as well as in the head, and meningeal symptoms usually quickly become obvious unless, as occasionally happens, they are masked from the first by those of a general septicemia.

The presence of inflammation of the meninges both of the brain and cord is shown by the occurrence of such various symptoms as optic neuritis inequality and fixation of pupil strabismus ptosis facial palsy and deafness by rigidity of the neck and muscles of the body causing retraction of the head and opisthotonos while among the more generalized signs of the nervous disturbance are convulsions delirium coma variations in the rhythms of respiration and heart beat with possibly some localized paralyse of limbs such as hemiplegia or paraplegia and other symptoms of nerve irritation such as have already been described in the account of tuberculous meningitis

Inflammation of the different structures of the eyes causing conjunctivitis corneitis iritis may take place and in some cases the destruction may be sufficiently extensive to cause permanent loss of sight Inflammations of the ears nose and lungs are also frequent and bronchopneumonia may be one of the serious complications Herpes round the mouth and a more generalized skin eruption in which there are small hemorrhages are common and it is from the appearance of the latter that the name of spotted fever has arisen The pulse and temperature are variable the latter often becoming of the intermittent type Swellings of joints may also take place

It will be seen how wide spread the effects are and that there is scarcely any system which may not be affected in an acute case In the fulminating cases the end may come within twenty four hours while in ordinary acute cases of fatal termination death is likely to occur within two or three weeks When the illness takes a favorable turn recovery takes place slowly and from time to time may be interrupted by a return of symptoms which again makes the outlook uncertain Sometimes the acute symptoms give way to those of a more chronic nature in which progressive emaciation and weakness are prominent features and recovery—if it takes place—is then liable to be accompanied by impairment of the mental faculties and hydrocephalus Such cases may last for some weeks during which the patient remains drowsy or semicomatose with incontinence of urine and feces and becomes reduced to a mere skeleton before death occurs from exhaustion or the results of intracranial pressure

Diagnosis

In the early stages the symptoms have to be differentiated from those of other acute infectious diseases and when the presence of meningeal symptoms has become definitely established the cerebrospinal meningitis has further to be distinguished from meningitis due to other forms of infection such as the tubercle bacillus pneumococcus and streptococcus

The characters of the cerebrospinal fluid are often decisive factors in the

diagnosis The fluid is increased in quantity and turbid in appearance with the formation of a slight sediment which increases in amount towards the later stages of the disease Microscopical examination of films taken from the fluid shows the presence of the meningococci and cases have been recorded in which other organisms have also been found in association with the meningococci The albumin is increased in amount and in the acute stage polymorphonuclear cells are present in considerable numbers Examination of the blood shows a considerable degree of leukocytosis and very occasionally the meningococcus has been isolated by culture or even found in directly stained blood films

Prognosis

The death rate during an epidemic is usually very high, especially in the case of children In individual cases the prognosis must depend upon the intensity of the general infection the signs denoting intracranial pressure and the course the illness is running The cases of fulminating onset nearly always terminate fatally and the outlook is almost equally bad in those in which the onset is acute and accompanied by early loss of consciousness and other signs of severe general toxemia

When the more acute symptoms have subsided the future becomes more difficult to predict for few of the symptoms have any direct bearing on the prognosis and patients who have been extremely ill may sometimes eventually make good recoveries

Treatment

Suspected cases should be isolated and possible carriers be looked for and treated when found The patient should be isolated and the same general methods that are used in the case of other infectious diseases should be adopted to prevent any spread of infection through the secretions bed clothes and utensils

No drugs appear to have any definite influence on the course of the disease but as in tuberculous meningitis urotropin may be given on account of its possible antiseptic action on the cerebrospinal fluid it has also been suggested as a prophylactic measure

Antimeningococcus serum as recommended by Flexner has proved of great benefit and the mortality of those having the serum has been reduced in some epidemics to a half or even a third as compared with that of patients to whom no serum was given A polyvalent serum is generally used although better results are claimed for monovalent sera corresponding to the type of the infecting coccus The serum should be given by the intraspinal method

A lumbar puncture is first performed and the amount of serum given can be adjusted to the amount of fluid withdrawn The serum should be introduced gradually by the gravity method but if for any reason a syringe is used the fluid must be injected very slowly and smoothly in order to avoid any irregular pressure

There is no distinct rule as to how often the injections should be repeated In an average case it is recommended to give from 10 c c to about 20 c c daily for the first four or five days but in the more severe cases it may be given at first twice daily Discretion must be used according to the course the disease appears to be taking but for general guidance it seems to be well to give as much during the early stages as is consistent with the amount of spinal fluid that can be safely removed provided there are no other obvious contraindications

While this treatment is being given it is well to watch the blood pressure a fall in which has been shown by Sophian to be an indication for stopping the injection

In the case of infants in whom hydrocephalus has developed if no fluid can be obtained by lumbar puncture it may if considered advisable be withdrawn for therapeutic or diagnostic purposes by tapping the ventricles through the anterior fontanelle by which route serum may also be introduced

Posterior Basic Meningitis

Etiology

The microorganism found in this variety is now recognized as being identical with that of epidemic cerebrospinal meningitis of which latter disease it is regarded as a sporadic form The disease most often occurs in young children up to about five years of age children debilitated by catarrh rickets and other forms of malnutrition are more apt to be attacked than those who are healthy the infection probably often reaches the membranes by way of the eustachian tubes and middle ear and the posterior area of the base of the brain is the part chiefly affected

Pathology

Examination after death shows the presence of inflammatory exudate chiefly over the posterior part of the base of the brain but sometimes extending on to the vertex and down the spinal cord The excessive exudation of fluid coupled with the impairment of its circulation in consequence of adhesions often gives rise to distention of the ventricles and consequent

hydrocephalus. The meningococcus can usually be obtained from the ventricular fluid.

Symptoms

The onset is usually acute; vomiting is apt to be an early symptom and the temperature is raised and irregular in course. Convulsions, general rigidity amounting to opisthotonos and retraction of the head frequently occur. Retraction of the head is one of the most prominent and charac-

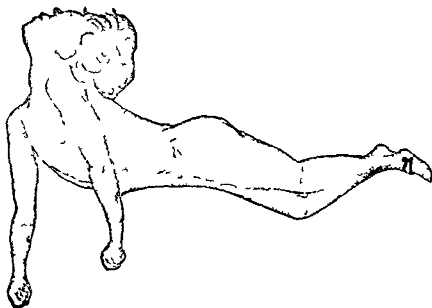


Fig. 3.—Case of Posterior Basic Meningitis showing Extreme Retraction of the Head.
(From Campbell Thomson's *Diseases of the Nervous System*.)

teristic features in this disease (Fig. 3). Optic neuritis, strabismus and alterations in the pupils may all be observed, but ocular symptoms are not met with so frequently as in tuberculous meningitis. Temporary or permanent blindness has been noted in many cases, which, if there is no optic neuritis, is probably to be accounted for by rise of general intracranial pressure. The rhythm of pulse and respiration is altered and in the later stages the child lies curled up in a semicomatose condition with symptoms largely resembling those of the later stages of tuberculous meningitis. The character of the cerebrospinal fluid is similar to that of the epidemic form, but towards the later stages of the illness the meningococcus is often more difficult to find and the fluid frequently also becomes more difficult to obtain.

Prognosis

The mortality of posterior basic meningitis is very high—eighty or ninety per cent —and in nonfatal cases unfortunately there is some impairment of the mental faculties in a considerable number of the survivors The duration of the illness is variable many cases lasting for several weeks during the latter part of which there are often prominent symptoms of *hydrocephalus*

Treatment

The general methods of treatment are similar to those described under the epidemic form Mercury and iodid have been recommended on account of their supposed influence on inflammatory processes but it is doubtful if any definite benefit is derived from any drugs

Serous Meningitis

In this form known also as wet brain the exudation is of a serous character and often more the nature of an edema than an inflammation It has been more particularly described in chronic alcoholics but it is met with in other conditions and recently cases which seem to correspond clinically to this condition have been sometimes observed to occur after an attack of *encephalitis lethargica*

The symptoms resemble those of other kinds of meningitis such as the suppurative form but are usually much less intense The cerebrospinal fluid although under pressure is free from organisms or from excess of cells The general signs of increased intracranial pressure such as headache vomiting and optic neuritis are among the principal symptoms and if as frequently happens the temperature is subnormal the condition may resemble that of cerebral tumor rather than meningitis With rest the symptoms may subside and considerable relief is also obtained sometimes by lumbar puncture If no improvement takes place and the vision is in danger of permanent deterioration an operation for cerebral decompression should be considered

Suppurative Meningitis

This form of meningitis is due to infection by streptococci with or without the presence of other organisms The meningitis may be part of a generalized infection but more usually it arises through an extension of suppuration

from neighboring areas, *e g* the mastoid, middle ear bony sinuses or by *the rupture of cerebral abscess into one of the lateral ventricles* The symptoms do not differ materially from those of other forms except that the convexity of the cerebral hemisphere is more liable to be attacked so that the cranial nerves are less likely to be affected—at any rate in the earlier stages—than in those varieties in which the base of the brain is the principal seat of the trouble Suppurative meningitis usually runs a rapid course and kills the patient within a few days

PNEUMOCOCCAL MENINGITIS

In this variety the pneumococcus is the predominant organism The infection of the meninges is generally secondary to a pneumococcal infection of lungs or elsewhere Like the suppurative form the pneumococcal variety usually runs an acute course and soon causes a fatal termination

Influenzal typhoid and other forms of meningitis have been described according to the predominance of the infective organism A description of syphilitic meningitis will be found in the section dealing with syphilis of the nervous system

CHAPTER XIV

INTRINSIC DISEASES OF THE SPINAL CORD

By JAMES COLLIER

Revision by W. RUSSELL BRAIN

Table of Contents

I

Myelomalacia. Softening of the Spinal Cord

The term "myelomalacia," which implies softening of the spinal cord, has been applied by some authors to those conditions of local destruction of the spinal cord which are consequent upon the cessation of blood supply and especially upon thrombosis of its blood vessels, as apart from the extensive local destructions which may result from inflammatory conditions. Such a distinction does not rest upon any logical pathological or clinical basis, for thrombosis and ischemia make up a part of the pathological process of all traumatic, inflammatory and pressure lesions of the spinal cord and may occur as terminal events in certain diseases of the spinal cord where vascular lesions are otherwise conspicuous by their absence. Therefore, since softening of the spinal cord may be the result of widely different pathological processes and since it does not constitute a definite clinical entity, it will suffice in this place to refer to those maladies in which it is chiefly met with.

Traumatic Conditions.—As the result of the intense vibration set up by the lines of force of high explosives bursting in the neighborhood of the spinal column, even without signs of external injury or signs of damage to the bones, the spinal cord may be found to be completely diffluent over several segments. The same result may be met with from the passage of a high velocity bullet through the spinal canal, whether the spinal cord be touched by the bullet or not, and again the same condition occurs from the vibration of an impact when a missile hits and lodges in the surrounding bone without directly involving the spinal canal or cord. A slighter degree of the same condition may be seen in fracture dislocations. When as the result of injury to the spinal column the spinal cord is torn across, the distal segment may soften completely, as in the following case. A child delivered with difficulty owing to extension of the aftercoming head presented a complete flaccid paraplegia from the seventh cervical level downwards and survived eight weeks. The spinal cord was found torn across at the seventh

cervical segment There was a fracture dislocation of the sixth cervical vertebra The distal segment of the cord was completely necrotic and had the appearance of a strip of wet wash leather There were no signs of thecal hemorrhage

Pressure Lesions—Pressure upon the spinal cord abrogates function chiefly by producing ischemia If the pressure be prolonged or severe necrotic softening occurs and the more readily if there be strangling of the segmental vessels which supply the cord and accompany each nerve root as in cases of syphilitic tuberculous or cancerous pachymeningitis or if there be coincident disease of the vessel walls as in syphilis and arteriosclerosis It must be borne in mind that the pressure may be exerted from within the cord as for example by the acute edema of the cord which is so important a factor in producing the rapid onset of paralysis in acute myelitis and syringomyelia where complete transverse softening may occur from the distention of a cavity Local patches of softening from strangling of segmental vessels are one of the chief causes of non recovery from the paraplegia of spinal caries when pressure has been relieved In intrathecal hemorrhage where the blood has been allowed to form a massive clot round the lower part of the spinal cord extensive softening may occur

Inflammatory Conditions—In acute spreading myelitis in which the spinal cord is infected with microorganisms secondarily to a general blood infection as may occur in smallpox gonorrhea dysentery etc the cord softens and may become diffluent In acute transverse myelitis softening depends upon the severity of the initial edema and its duration the degree of obliterative arteritis present and the consequent thrombosis that may occur It may be largely avoided by the energetic and early application of antisyphilitic treatment

Terminal Softening in Progressive Diseases—In certain progressive diseases of the spinal cord extensive thrombosis of the vessels with softening may occur For example in a case of subacute combined degeneration which had been under my observation for several years complete flaccid paraplegia occurred a fortnight before death The most extensive thrombosis of the cord was found below the eighth dorsal level with complete necrosis of the distal segment throughout A similar condition is not infrequently seen in paraplegia from spinal caries

Senile Paraplegia—This condition which is not very rare and in which spasticity of the lower extremities with weakness comes on gradually in later life and does not as a rule reach a severe degree has been attributed to ischemia and even to softening of the spinal cord from arteriosclerosis and the failing circulation of old age by Moxon who first described it The pathology of these cases seems by no means certain and there are few records of their anatomy It seems unlikely that any appreciable softening can occur

on account of the slightness of the paraplegia and the absence of any sensory loss Gowers doubted whether they were spinal in origin at all and attributed some to the occurrence of cortical changes in the brain while others he placed in the category of paralysis agitans From the occasional occurrence of definite mental failure a cerebral site for the lesion is likely in some of the cases In one case clinically belonging to this class laminectomy revealed ivory like exostoses narrowing both the spinal canal and the intervertebral foramina and the case was obviously one of a slow pressure lesion

II

Progressive Muscular Atrophy

This is a disease of gradual onset which may develop at any age from puberty onwards and in which the anatomical findings consist invariably whatever be the clinical picture of three orders (1) a progressive degeneration shrinkage and disappearance cell by cell of the upper motor neurons or cells of Betz in the ascending frontal convolution with consequent degeneration of the corresponding fibers in the pyramidal tracts (2) a similar atrophy cell by cell in the lower motor neurons with corresponding degeneration of motor fibers in the peripheral nerves and atrophic degeneration of the muscles innervated by the affected cells (3) a diffuse atrophy of the white matter of the spinal cord the posterior columns conspicuously excepted so that in transverse sections of the spinal cord stained by Weigert s method a characteristic picture is seen (Fig 1) the darkly stained normal posterior columns contrasting conspicuously with the pale stained and partly degenerate white matter of the anterior antero lateral and lateral regions

The clinical picture is one of gradually oncoming weakness and disability due either to atrophy of the muscles from the lower motor neuron lesion in which case the paralysis is flaccid and atrophic, or to spastic paralysis of the muscles from the upper motor neuron lesion in which case the paralysis is spastic without atrophy or to the combined lesion of both upper and lower motor neurons in which case the paralysis is both spastic and atrophic and the muscular atrophy never becomes complete Fibrillary twitchings of the muscles are always present and form an important diagnostic feature Any of the skeletal muscles may be affected from the ocular muscles to those of the feet

A most mysterious feature of the disease is the non correspondence between the anatomical findings and the symptomatology In the first place though the upper motor neuron lesion is constant in all cases many

cases run their course without the slightest external evidence that the pyramidal system is involved Secondly no symptoms develop in any of

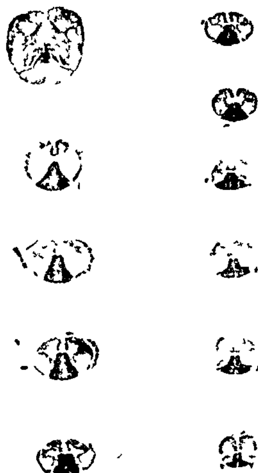


FIG 1 —Sections of the spinal cord and medulla from a case of progressive muscular atrophy stained by the Weigert Pal method showing the diminution in size of the ventral horns in the cervical region and the widely spread diffuse degeneration of all the white matter in front of the posterior horns which is best marked in the region of the pyramidal tracts The posterior columns alone are normal From a photograph by Dr Greenfield

the cases corresponding with the very extensive degeneration of the anterior and anterolateral columns of the cord

The clinical aspect varies greatly according as the incidence of the palsy is upon the muscles supplied by the brain stem or upon the muscles of the trunk and limbs and again according as the atrophic element or the spastic element is present alone or as both coexist in the same region or in different regions of the body

The following are the usual clinical types but it must be borne in mind that every transition between these types may be met with

A With incidence upon the muscles supplied from the brain stem
Progressive Bulbar Paralysis (Dumenil, 1859)
1 Pure Atrophic Bulbar Paralysis
2 Spastic Atrophic Bulbar Paralysis
3 Pure Spastic Bulbar Paralysis (Duchenne's type 1860)

B With incidence upon the muscles of trunk and limbs
1 Pure Atrophic Type
(a) Local and slowly progressive
(b) General and rapidly progressive
2 Spastic Atrophic Type Amyotrophic Lateral Sclerosis (Charcot)
(a) The spasticity and atrophy are coincident in the same muscles
(b) The atrophy affects the upper limb and the spasticity the lower limb
3 Pure Spastic Type This is more commonly seen as an early stage of amyotrophic lateral sclerosis where the spasticity of the lower extremities precedes the atrophy of the upper extremities by some months or years

C Mixed Bulbar and Spinal Forms

Etiology

The earliest age incidence has been at twelve years and several cases have been recorded which developed the disease at that age As age advances, the incidence of the malady becomes more frequent until it attains a maximum between the ages of thirty and forty years after which there is a slow decline It does not commonly commence in advanced age but one case has come under the writer's observation which commenced at the age of seventy seven years The progressive muscular atrophy of infants of spinal origin first described by Werdnig and Hoffmann is recorded as a distinct malady

Males are affected three times as frequently as are females but in the cases occurring before the age of twenty five years the females predominate Neither age nor sex seems to influence the type of the disease Heredity only

rarely influences the disease but occasionally several members of a family may be affected and several instances have been recorded in which parental disease has been followed by the development of this malady at much the same age in the child

Such antecedents as mental distress and anxiety overwork exposure debilitating illnesses war strain and so forth are often to be met with in the history of the patients and are probably only in relation to this disease as the immediate exciting cause of the appearance of symptoms Injury is much more important and while a rare causal factor cases are not very uncommon in which progressive muscular atrophy of typical course immediately follows upon an injury and commences first in the region of the injury I have twice seen this malady commence in the muscles of the back after a blow upon the spine Commencement in a limb which has recently been injured is more frequent and general traumatic influences such as are occasioned by a fall not very uncommonly precede the onset of symptoms in patients of later years and the course of the disease in such cases is likely to be rapid

Syphilis seems to be in definite causal relation with some of the cases A positive Wassermann reaction both in the blood and in the cerebro spinal fluid is found in a much larger proportion of the cases than give any history of syphilitic infection Further quite a number of instances of the supervention of a typical progressive muscular atrophy in cases of tabes has been observed and recorded at the National Hospital London Again I have seen a typical case develop general paralysis of the insane Among the many conditions of atrophic paralysis which may occur in syphilis of the nervous system are some the nuclear ophthalmoplegias and the nuclear laryngoplegias for example which are certainly due to a slow primary atrophy of the motor neurons and it is reasonable to argue that a similar process may affect the motor neurons widely and produce a typical progressive muscular atrophy It has been freely stated that progressive muscular atrophy of syphilitic origin differs from the non syphilitic forms in its lack of symmetry and in its course but this certainly does not hold good for very many of the cases which show a positive Wassermann reaction

Lead poisoning seems to be a very doubtful factor I have never seen nor have I been able to find in the numerous records of the National Hospital any cases in which undoubted lead poisoning has been followed by typical progressive muscular atrophy Gowers gives the opinion that lead poisoning may cause a muscular atrophy which is similar in seat and features to progressive muscular atrophy but that this is not progressive when its cause has ceased to act It must be borne in mind that because a man is a worker in lead it does not follow that a disease which he may develop is caused hereby In a large majority of all cases of progressive muscular atrophy no causal factors whatever can be discovered

Morbid Anatomy

To the naked eye a cross section of the spinal cord may show some diminution in size of the ventral horns which often present a curiously pink or rose colored appearance The essential lesion is a primary degeneration of the cells of the ventral horns of the spinal cord and in the homologous motor nuclei of the brain stem namely the hypoglossal facial trigeminal and oculomotor nuclei It is important to note that degeneration is seldom found in the nucleus ambiguus or in the glossopharyngeal nuclei Coupled with the degeneration of the lower motor neurons is a degeneration of the upper motor neurons of the pyramidal system which was first traced upward to the ascending frontal convolution by Kojewnikoff in 1883 In the ventral horn cells the degeneration is evidenced by a gradual shrinking in size of the cells which lose their dendrites and become oval or spherical in shape The Nissl bodies slowly disappear and only in rare and rapid cases is definite chromatolysis seen The nuclei dwindle and become irregular and distorted Very striking and constant is a great increase of the yellow intracellular pigment which is usually present in a single mass near the nucleus or at the pole of the cell As this pigment increases in bulk it gradually displaces the nucleus and the other elements of the cell until the degenerate cells come to consist of a mass of pigment contained within the cell wall with a distorted nucleus lying to one side Invasion of the pigmented cell remnants by neurophages completes the destruction and in a late stage groups of such neurophages laden with nerve cell pigment alone mark the site from which the nerve cell has disappeared

Consequent upon the degeneration of the ventral horn cells the *reticulum* of myelinated fibers in the gray matter of the ventral horn disappears the collaterals coming from the dorsal roots alone remaining intact The destruction of the elements of the ventral horn is followed by a secondary proliferation of the neuroglia with increase of the nuclei and fibrillar elements and especially in cases of rapid course there is engorgement of the blood vessels with a moderate degree of small round celled infiltration of the vascular walls The presence of such vascular changes has led to the hypothesis that they constitute the primary lesion in progressive muscular atrophy and that the nervous degeneration is secondary thereto but there can be no doubt whatever that the converse is the fact and that the vascular changes are entirely secondary to the primary degeneration of the nerve elements

The dorsal and lateral horns are almost invariably intact but degenerative changes are sometimes seen in the cells of Clarke s column from which degeneration of the spinocerebellar tracts necessarily results The affection of the motor nuclei of the brain stem in the bulbar cases is in every

way similar to that of the ventral horns The degeneration of the motor nerves which take origin from the degenerate ventral horn cells often proceeds *pari passu* with the degeneration of the cells But in some cases this is conspicuously and very mysteriously not the case for though there may be intense degeneration in the ventral horn cells and in the intra medullary motor roots and in the muscles there may be complete absence of any signs of degeneration in the motor fibers of the extramedullary roots and peripheral nerves

The affected muscles are soft and toneless and the muscle fibers are found irregularly degenerated bundles of normal fibers and of degenerating fibers until the atrophy is complete being found side by side The characteristic change is that the affected fiber shrinks to a caliber much less than the normal The transverse striation usually persists and the muscles stain much more deeply than is normal with logwood The nuclei are much increased and as the degenerating fibers waste and disappear completely the positions which they originally occupied are marked by clumps of such nuclei which remain in the connective tissue Occasionally a few of the fibers increase in size and undergo regressive changes such as invasion of the sarcoplasm by the nuclei fission and vacuolation As is usual in all low tissue degenerations fibrosis and local arteriosclerosis accompany the atrophy of the muscle fibers

The pyramidal neurons (cells of Betz) which characterize the precentral cortex undergo a degeneration very similar to that of the ventral horn cells but with this difference which was first pointed out by Oppenheim that the earliest structural changes are found in the most distal part of the pyramidal fibers and that subsequently these fibers die back towards their cells of origin in the cerebral cortex The degeneration of the upper motor neurons never proceeds to the complete destruction of anything like all the pyramidal fibers

As has been emphasized above there is invariably a very considerable diffuse atrophy of the ventrolateral columns of the spinal cord and this is usually more marked in the shorter fibers which surround the ventral horn and which take origin from the smaller cells of the dorsal portions of that horn and connect the segments of the spinal cord at different levels one with the other Degeneration of nerve fibers is found also fairly constantly in the ventral commissure in both spinocerebellar tracts in the fillet tectospinal tracts rubrospinal tracts and in the dorsal longitudinal bundle and in the mesial part of the corpus callosum the degeneration in the latter position being presumably that of collaterals of the pyramidal fibers

The pathological nature therefore of progressive muscular atrophy is a widely scattered degeneration of nervous elements not even confined to the motor systems though these are in the main affected since the afferent

spinocerebellar tracts are constantly found degenerate. The cause for such degeneration is unknown. The primary neuronic degeneration which occurs in syphilis of the nervous system suggests that a toxic state may induce the degeneration which causes progressive muscular atrophy but apart from the facts that some few of the cases have active syphilis and that in isolated cases lead poisoning has a doubtful influence there are no facts which support this hypothesis. Moreover a great many of the subjects of this disease are of the robust type with a particularly clean antecedent bill of health. A deprivation hypothesis from internal secretory failure though fascinating does not as yet rest upon any knowledgeable basis. Strumpell has postulated an inherent tendency to degeneration an abiotrophic constitution but such a condition is purely hypothetical. Erb and others have assumed that the causation is essentially traumatic upon the evidence of some of the cases commencing after injury and from the occasional occurrence of the disease in persons who have suffered from acute polio myelitis in childhood but it is impossible to conceive how an injury can cause so widely spread a degeneration.

Clinical Aspect

The following description of the clinical features is based upon an analysis of five hundred cases which have come under observation at the National Hospital London.

The onset is in most cases very gradual but it may be more rapid and severe incapacity may result in the course of a few months. In rarer cases a severe degree of paralysis may develop in the course of a few days and in such cases it is not uncommon to see the most remarkable temporary improvement. The nature of the onset as a rule indicates the course which the malady will pursue. A very slow onset is followed by a very slowly advancing disease often interrupted by long stationary periods whereas the more rapid the commencement the quicker will be the advance and the sooner will a fatal issue occur.

Accompanying and sometimes preceding the onset and not infrequently conspicuous during the early states of the disease are certain sensory symptoms which from the confusion in diagnosis they may cause and from the scant attention which has been paid them in descriptions of the malady hitherto deserve emphasis. These symptoms are confined to the regions where the wasting first appears and consist in a subjective feeling of stiffness and uselessness much increased when the limb or the body is cold. Or there may be dull aching pains intermittent neuralgic pains which may be severe or a sensation of coldness or numbness which may be intense. Less commonly tingling may be present. Painful cramp in the muscles which are

about to be affected is comparatively common There is usually no objective loss of sensibility but in several cases I have seen well marked relative analgesia over the eighth cervical and first dorsal areas when the atrophy commenced in the hands and over the fifth lumbar and first sacral areas when the atrophy commenced in the feet and this occurred in cases where syphilis could be absolutely excluded and where the subsequent course of the cases and the pathological examination proved them to be typical examples of the disease These sensory symptoms though confusing at first are always transient and disappear as the disease progresses with the exception of aching pain and painful cramps which may recur from time to time

The *muscular wasting* which constitutes the most characteristic feature of the disease may commence in any group of the skeletal muscles whatsoever It may be first manifest in such rare situations as the facial muscles (Gowers) intercostal muscles muscles of the back and abdominal muscles The commonest situation is in the muscles of the upper limb where the distal muscles (intrinsic muscles of the hand) or the proximal muscles (deltoids spinati etc) are first affected in about an equal number of cases In the hand the muscles of the thenar eminence are the first to waste and this is followed by atrophy of the hypothenars of the lumbricals and of the interossei with the usual flattening of the palm exposure of the flexor tendons in the palm from loss of the bulk of the lumbricals hollowing of the interosseous space and a tendency to the griffin s paw" attitude of the hand The main en griffe is never so marked in this disease as in paralysis of the ulnar nerve syringomyelia etc because the wasting soon affects the long flexors of the fingers and further contractures of the affected muscles are not well marked in progressive muscular atrophy As the wasting spreads to the muscles of the forearm the flexors are usually affected before the extensors

When the upper arm is primarily affected the wasting is first seen most often in the deltoids whence it spreads upward involving the spinati and the muscles attaching arm to scapula and arm and scapula to trunk Among these muscles some tend to escape the atrophy relatively or to be affected much later than other and these are the triceps the latissimus dorsi the lower half of the pectoralis major the levator anguli scapulae and especially the upper half of the trapezius which for this reason was called ultimum moriens" by Duchenne To this general rule there are frequent exceptions and examples may be met with in which these usually resistive muscles and even the upper part of the trapezius may be the first affected In the limbs the wasting always commences in one limb but soon spreads to the corresponding limb of the opposite side and tends ultimately to become symmetrical But in less common cases the disease may be manifest and

become extreme in one limb alone for a very long time before there is extension to the opposite limb and there is one verified case recorded in which the disease remained strictly unilateral

The attention of the patient may be first drawn to his malady by the altered appearance produced by the atrophy and this is more common when the commencement is in the hands where the subcutaneous tissue is thin and the region constantly in view Or the disability consequent upon the weakness may be noticed first and this is always the case where the commencement is in the bulbar muscles and usually also where the muscles of the legs proximal muscles of the arms and trunk muscles are first involved Lastly the fibrillation may be so marked as first to attract notice

The *loss of power* which accompanies the muscular wasting is as a rule commensurate with the wasting and does not become absolute until the atrophy is complete To this rule however there are two very important exceptions *In the first place when the affected muscles are both tonic* from the upper motor neuron lesion and atrophic from the ventral horn cell lesion the tonic atrophy of Gowers the loss of power is always much greater than can be accounted for by the degree of wasting present It is a remarkable and entirely unexplained fact that when this tonic atrophy is present the muscles never completely waste whereas in flaccid atrophy they waste completely if the patient survive sufficiently long In the second place and in a minority of the cases a complete flaccid paralysis often of considerable extent involving perhaps all the muscles of the hand and forearm or all the muscles of the shoulder and upper arm occurs as the initial phenomenon and precedes any sign of wasting This initial flaccid *paralysis without wasting generally comes on rapidly* It is not accompanied by any fibrillation and often it remits to a very considerable extent before any wasting or fibrillation appears When the disease commences with initial flaccid paralysis without wasting it is usually rapid in its course any temporary improvements notwithstanding This initial flaccid paralysis without wasting especially if it improves temporarily may give rise to great difficulty in diagnosis for it generally occurs in one limb only and its rapid development and in some cases a conspicuous improvement may give rise to the impression of a gross organic lesion of the ventral horn or ventral roots and to hopes of recovery which are falsified later

The disability which progressive muscular atrophy produces in the limbs is always much more marked when the limbs are cold and conversely There may be an appearance of vasomotor paralysis redness blueness and some swelling of the periphery but this seems to occur much more as the result of the continual pendant position of the hands when the muscles which flex the elbow and which raise the shoulder are affected than as the result of any definite vasomotor palsy In the regions where the muscular

atrophy is apparent the fat and subcutaneous tissues also waste slowly and progressively and in all but the rapidly progressive cases this wasting is conspicuous

Next in order of frequency to initial wasting in the upper extremities comes the incidence of the disease upon the muscles concerned in facial expression articulation mastication and deglutition and in lesser degree upon the muscles of phonation and the disease may be confined to these muscles throughout the whole of its course From the widely different clinical picture resulting and from the fact that all these muscles are supplied from the brain stem and upper two segments of the spinal cord this form of the disease has borne the name of progressive bulbar paralysis or labio glossolaryngeal paralysis *Here the wasting commences in the intrinsic* muscles of the tongue and spreads thence to the orbicularis oris to the extrinsic muscles of the tongue pharynx and larynx to the muscles of mastication and eventually but in less degree to the facial muscles generally but only in rare cases are the oculomotor muscles affected

The intrinsic muscles of the palate the constrictors of the pharynx the intrinsic muscles of the larynx and the muscle of the esophagus are little affected I have in a series of cases examined microscopically all the muscles concerned in the acts of deglutition and phonation and have found these muscles conspicuously exempt from atrophy This seems at first an anomalous and astonishing fact considering how great and important are the troubles with deglutition in bulbar paralysis But the anomaly disappears at once when one considers that the muscles which are concerned with buccal deglutition are the muscles of the tongue the muscles forming the floor of the mouth including the mylohyoid and the digastric the muscles which raise and lower the jaw and the muscles of the lips Further the muscles which are most important in pharyngeal deglutition are those which raise and lower the hyoid bone and larynx as a whole and these are the stylohyoid and stylopharyngeus the palatoglossus and palatopharyngeus the geniohyoid thyrohyoid sternohyoid sternothyroid and omohyoid All these muscles are early and severely affected in bulbar paralysis and when these muscles fail the intrinsic muscles of the palate are unable to shut off the nasopharynx the constrictors of the pharynx *are entirely unable to perform the act of deglutition and the intrinsic* muscles of the larynx though phonation is never lost are unable since the larynx is unfixed by the extrinsic muscles to modulate the tone of the voice The very active pharyngeal reflex and the well known great difficulty in using the laryngoscope on account of spasm of the pharynx in the subjects of this disease are very good clinical evidence that the pharyngeal constrictors are not affected

The earliest physical sign of bulbar paralysis is the loss of the finer

movements which are essential for correct articulation and consequently a slurring dysarthria develops and increases and the consonants become less and less distinct until they are inaudible The failure of the palate to close upon the posterior pharyngeal wall begets a nasal element in the voice Later the patient becomes unable to interrupt his blast at any of the stop positions and his utterance becomes a long, moaning monotonous inarticulate sound His phonation remains but he cannot alter its pitch nor divide it into parts of speech except by taking a fresh breath The orbicularis oris is early affected and the lips lose their firmness and become thin and as this muscle weakens, the unopposed retractors of the angles produce a wide straight mouth both at rest and in emotional action Whistling and pursing up the lips become impossible and ultimately there is much dribbling of saliva which can be neither retained by the lips nor swallowed The tongue shows fine fibrillation and as it wastes it loses its point becomes rounded and is protruded with difficulty Its surface becomes dimpled and facetted and in the end consists solely of the covering mucous membrane the glands and fibrous tissues and lies motionless in the floor of the mouth resembling a crinkled mushroom The muscles of mastication all become affected The bite becomes feeble and the mouth cannot be opened against resistance In the late stages the jaw drops and the mouth is constantly open The combined weakness of tongue and buccinators makes it very difficult for the patient to keep his food between his teeth in mastication and often he aids his disability by digital pressure upon the cheeks Nasal regurgitation is not uncommon

The difficulty in swallowing is greatest with fluids for these require quick action and is next greatest with lumpy solids for these require powerful action It is least with food of a porridge like consistency and this should be carefully borne in mind in the feeding of the patients

The other muscles of the face are affected later and to a much less severe degree than is the orbicularis oris It is as if there was a physiological selection on the part of the disease for the nervous mechanism subserving mastication and deglutition Still in the majority of cases there are bilateral general facial weakness and wasting which with the peculiar mouth and dropping jaw produce a characteristic facies which can be instantly recognized If the upper facial muscles are tested by raising the eyelid with the finger against resistance invariably they will be found to be weak Only in very rare cases does the atrophy extend to the oculomotor muscles As in the paralysis of the limbs so also in bulbar paralysis concomitant signs of both upper motor neuron lesion and of lower motor neuron lesion may exist When such tonic atrophy of the bulbar muscles is present the symptomatology and clinical appearance are the same as have been above described in the simple atrophic form with the exception that the jaw jerk

and the other muscle jerks of the bulbar region which are absent in the latter condition are brisk in the tonic atrophic form And further it must be remembered that the additional element of spastic paralysis adds greatly to the degree of the paralysis as a whole

In less common cases of progressive bulbar paralysis the upper motor neuron lesion alone is in evidence and the bulbar paralysis is purely spastic Here the symptomatology as regards articulation deglutition etc is the same and the facial aspect identical with that of the simple atrophic and tonic atrophic form The muscle jerks are brisk The appearance of the tongue however is quite different it is smooth narrow stiff and drawn into a narrow compass by the spasm of the muscles composing it It appears too small for so large a mouth There is no fibrillation and the muscles are nowhere wasted

The muscles of the back of the neck the splenius, complexus etc are not uncommonly the first muscles to be affected with the wasting of progressive muscular atrophy There is increasing difficulty in extending the head which drops forward causing a characteristic attitude Associated with this attitude of the head is a constant overaction of the frontales which raise the brows to clear the line of vision when the head is dropped forward so giving rise to a permanently furrowed brow The loss of substance in the muscles of the back of the neck together with the dropping forward of the head causes the lower cervical and upper dorsal spines to stand out in undue prominence and to give an appearance somewhat resembling that of an angular curvature

Primary affection of the lower extremities is much less common than that of the upper extremities bulbar region or neck muscles The anterior tibial and peroneal muscles are usually attacked first and less commonly the quadriceps The clinical type is that of flaccid atrophy in most of the cases Tonic atrophy which is so common in the upper limbs and in the bulbar region is rare in the legs

Spasticity without atrophy from the upper motor neuron lesion alone is very common in the lower extremities It forms a characteristic part of the frequently occurring clinical type of amyotrophic lateral sclerosis in which the upper extremities or bulbar region are affected with atrophic paralysis and the legs with spastic paralysis In this common combination the atrophic paralysis is usually of the tonic type and much less frequently of the simple flaccid type

Spasticity from the upper motor neuron lesion may develop in the lower extremities long before there are any signs of atrophic paralysis elsewhere from the lower motor neuron lesion and such cases present the physical signs of a primary lateral sclerosis Therefore it cannot be too strongly borne in mind that any case presenting the features of a primary lateral

movements which are essential for correct articulation and consequently a slurring dysarthria develops and increases and the consonants become less and less distinct until they are inaudible The failure of the palate to close upon the posterior pharyngeal wall begets a nasal element in the voice Later the patient becomes unable to interrupt his blast at any of the stop positions and his utterance becomes a long, moaning monotonous inarticulate sound His phonation remains but he cannot alter its pitch nor divide it into parts of speech except by taking a fresh breath The orbicularis oris is early affected and the lips lose their firmness and become thin and as this muscle weakens the unopposed retractors of the angles produce a wide straight mouth both at rest and in emotional action Whistling and pursing up the lips become impossible and ultimately there is much dribbling of saliva which can be neither retained by the lips nor swallowed The tongue shows fine fibrillation and as it wastes it loses its point becomes rounded and is protruded with difficulty Its surface becomes dimpled and facetted and in the end consists solely of the covering mucous membrane the glands and fibrous tissues and lies motionless in the floor of the mouth resembling a crinkled mushroom The muscles of mastication all become affected The bite becomes feeble and the mouth cannot be opened against resistance In the late stages the jaw drops and the mouth is constantly open The combined weakness of tongue and buccinators makes it very difficult for the patient to keep his food between his teeth in mastication and often he aids his disability by digital pressure upon the cheeks Nasal regurgitation is not uncommon

The difficulty in swallowing is greatest with fluids for these require quick action and is next greatest with lumpy solids for these require powerful action It is least with food of a porridge like consistency and this should be carefully borne in mind in the feeding of the patients

The other muscles of the face are affected later and to a much less severe degree than is the orbicularis oris It is as if there was a physiological selection on the part of the disease for the nervous mechanism subserving mastication and deglutition Still in the majority of cases there are bilateral general facial weakness and wasting which with the peculiar mouth and dropping jaw produce a characteristic facies which can be instantly recognized If the upper facial muscles are tested by raising the eyelid with the finger against resistance invariably they will be found to be weak Only in very rare cases does the atrophy extend to the oculomotor muscles As in the paralysis of the limbs so also in bulbar paralysis concomitant signs of both upper motor neuron lesion and of lower motor neuron lesion may exist When such tonic atrophy of the bulbar muscles is present the symptomatology and clinical appearance are the same as have been above described in the simple atrophic form with the exception that the jaw jerk

and the other muscle jerks of the bulbar region which are absent in the latter condition are brisk in the tonic atrophic form And further it must be remembered that the additional element of spastic paralysis adds greatly to the degree of the paralysis as a whole

In less common cases of progressive bulbar paralysis the upper motor neuron lesion alone is in evidence and the bulbar paralysis is purely spastic Here the symptomatology as regards articulation deglutition etc is the same and the facial aspect identical with that of the simple atrophic and tonic atrophic forms The muscle jerks are brisk The appearance of the tongue however is quite different it is smooth narrow stiff and drawn into a narrow compass by the spasm of the muscles composing it It appears too small for so large a mouth There is no fibrillation and the muscles are nowhere wasted

The muscles of the back of the neck the splenius complexus etc are not uncommonly the first muscles to be affected with the wasting of progressive muscular atrophy There is increasing difficulty in extending the head which drops forward causing a characteristic attitude Associated with this attitude of the head is a constant overaction of the frontales which raise the brows to clear the line of vision when the head is dropped forward so giving rise to a permanently furrowed brow The loss of substance in the muscles of the back of the neck together with the dropping forward of the head causes the lower cervical and upper dorsal spines to stand out in undue prominence and to give an appearance somewhat resembling that of an angular curvature

Primary affection of the lower extremities is much less common than that of the upper extremities bulbar region or neck muscles The anterior tibial and peroneal muscles are usually attacked first and less commonly the quadriceps The clinical type is that of flaccid atrophy in most of the cases Tonic atrophy which is so common in the upper limbs and in the bulbar region is rare in the legs

Spasticity without atrophy from the upper motor neuron lesion alone is very common in the lower extremities It forms a characteristic part of the frequently occurring clinical type of amyotrophic lateral sclerosis in which the upper extremities or bulbar region are affected with atrophic paralysis and the legs with spastic paralysis In this common combination the atrophic paralysis is usually of the tonic type and much less frequently of the simple flaccid type

Spasticity from the upper motor neuron lesion may develop in the lower extremities long before there are any signs of atrophic paralysis elsewhere from the lower motor neuron lesion and such cases present the physical signs of a primary lateral sclerosis Therefore it cannot be too strongly borne in mind that any case presenting the features of a primary lateral

sclerosis in an adult may eventually prove to be one of progressive muscular atrophy It is a mysterious and hitherto inexplicable fact that when pure spasticity develops in any region in progressive muscular atrophy the muscles of that region never subsequently become atrophic but remain spastic and unwasted to the end We have already seen this same principle obtain in a relative degree where spasticity and atrophy (tonic atrophy) come on simultaneously in any region for then the muscles never waste completely whereas in simple atrophy complete destruction of all the muscle fibers is the rule

Wherever the site of commencement of progressive muscular atrophy may be it invariably spreads to other regions sometimes slowly and with periods of arrest which may last for years sometimes with remarkable rapidity The manner of spreading is usually in terms of the contiguity of the affected elements in the nervous system but it is sometimes in terms of the physiological association of the muscles as is commonly seen in the bulbar forms of the malady Not rarely it breaks out in a fresh place at some distance from the region primarily involved For example when the hands are first affected, it may appear in the shoulder muscles or in the bulbar region without any affection of the intervening muscles

When the disease is definitely installed the appearance of fibrillation in any muscles otherwise unaffected is a sure sign that atrophy will shortly commence in those muscles

According to the method of advance shown by the disease cases of progressive muscular atrophy fall into two groups which it is important to distinguish In the first group the atrophy spreads locally and slowly and remains confined to one region of the anatomy during most of the course of the malady These cases are always of the simple atrophic type and they usually survive a long time As an example a girl of seventeen years developed progressive muscular atrophy in the hands which slowly spread to the forearms upper arms and shoulders Twenty five years later she has complete atrophy of every muscle of the upper extremity but there is not the slightest affection of the lower extremities trunk or bulbar region Such cases however tend to become general just before the end In contrast with the local type of the affection is the group in which the manifestation commencing locally spread within a comparatively short time to many parts of the anatomy or even become universal The spread may be very rapid and the end may occur in a few months or it may be slower but it is unusual for any of the cases forming this group to survive for more than eighteen months This group comprises (1) the generalized cases of simple flaccid atrophy (2) all the cases of amyotrophic lateral sclerosis and (3) most of the bulbar cases

Fibrillation is a most important symptom of the disease and is an

associate of the muscular atrophy It seems to be the expression of degeneration which is occurring in the yet living and functioning nerve cell It precedes the wasting of the fibers and is a sure herald of the advent of wasting in this disease It ceases to occur when the muscle is completely wasted and is not seen when the atrophy is not progressing The twitching of the muscle fibers is usually fine and causes no movement of the limb but sometimes it may be sufficiently powerful to cause constant spontaneous involuntary movements of the fingers It is particularly evident in the tongue and lips when these are involved

On account of the importance of fibrillation as a diagnostic sign of progressive muscular atrophy it is important here to consider those other conditions in which it is met with clinically It occurs in syringomyelia and in peroneal atrophy but only when the muscular atrophy is progressing and therefore it is only an occasional symptom in either disease It is often very marked in cases of interstitial neuritis (sciatica etc) It occurs in a most magnified and conspicuous form in certain conditions of gastroenteritis and is presumably due to an intoxication and to this form of fibrillation the term myokymia has been applied It is not met with in polyneuritis poliomyelitis myopathy nor in the common gross lesions of nerve trunks nerve roots or spinal cord

The *electrical reactions* of the affected muscles vary according to the degree of degeneration Since normal and degenerate fibers are stimulated side by side in the affected muscle there will be some lowering of the response to faradism with a tendency to a polar change This is known as the "mixed reaction" and it is common to all diseases in which muscle degenerates fiber by fiber Faradic excitability lessens as more of the muscle fibers degenerate and when degeneration is complete all electrical excitability is lost The excitability of the affected muscles to direct mechanical stimuli such as percussion is increased so long as any living muscle remains

Contractures are conspicuous by their absence in this disease which is thus strongly contrasted with peroneal atrophy and some other muscular atrophies It is true that a claw hand may be seen in the early stages when the intrinsic muscles of the hands are affected but this is due to the action of the unopposed long flexors and extensors and it disappears entirely when the latter muscles become affected If the atrophy become complete in a whole limb the end result is that the limb is flail like and without contracture

Pupils —Inequality of the pupils is of frequent occurrence and it is said to be more common when the hands are affected and that the smaller pupil is upon the side of the hand most affected the explanation being that the lesions of the eighth cervical and first dorsal segments have disturbed the cilio spinal path which traverses those segment However this may be it

is certain that typical cervical sympathetic paralysis does not occur in progressive muscular atrophy unless tabes be coincident Ectopia and variable unroundness of the pupils are often met with The Argyll Robertson pupil has been met with fairly often and in several cases at least where syphilis could be definitely excluded It must be remembered in this connection that a proportion of the subjects of this disease have had syphilitic infection and show a positive Wassermann reaction and further that the coincidence of tabes and progressive muscular atrophy in the same subject is by no means rare and in such cases any of the signs produced by the syphilitic lesions of tabes may arise

Mental alterations are constantly present in the cases in which the bulbar region is affected Emotional instability and hyperexcitability are the usual changes The patient is easily excited to tears or to laughter by trivial causes and when so excited cannot control his expression of emotion He himself feels little joy or grief during the paroxysms of laughing or crying Such instability in the expressions of emotion is a symptom of many varied lesions of the brain stem In the later stages of all forms of the disease mentality becomes considerably reduced and this is not surprising considering the widely spread degenerations of the nervous system which occur towards the end of the course of the disease

Sphincters —In the majority of the cases these are not affected but every now and then dysuria in any of its forms occurs and it may occur early in the course of the malady and it may be severe It s more common in the typical amyotrophic lateral sclerosis and has been attributed to the pyramidal lesion but it is not confined to the spastic cases and it may equally be due to the considerable changes found in other anterolateral tracts in the cord It may further be the result of coincident syphilitic lesions Loss of sexual power is very common

Reflexes —The superficial reflexes are modified in this disease on the one hand by spasticity when this is present and on the other by the muscular atrophy which may prevent response in the affected muscles The pharyngeal reflex in bulbar cases is usually brisk notwithstanding the statement to the contrary which most antecedent writers upon this subject have recorded but the response is not the normal response involving all the muscles concerned in deglutition for these are atrophied and paralyzed it is confined to the constrictors of the pharynx and the muscles of the palate with the feeble cooperation of such of the somatic bulbar muscles as are still able to act

The abdominal reflexes are diminished or lost in the spastic cases and in those cases where the atrophy is incident upon the muscles of the abdominal wall The plantar reflexes are usually of the extensor type when the leg are spastic but this does not always obtain for there may be definite rigidity

of the leg with brisk knee jerks and foot clonus together with a persistent flexor response The muscle jerks disappear from the affected region in simple atrophic cases *pari passu* with the wasting of the muscles In cases of tonic atrophy they are everywhere increased even in regions where the atrophy is severe and in this type of the malady they never disappear This is very well seen in tonic bulbar cases where a jerk can be elicited from each of the facial muscles by stretching the fibers with the finger and then tapping the finger The same increase of the muscle jerks occurs in the purely spastic cases

Course

The nature of the disease is to progress and to extend its area of invasion until a fatal issue is reached The progress may be rapid and the end may be reached in a few months or it may be slow and many years may elapse before death occurs The local types of slow onset are the most gradual in their development and these are often characterized by periods of arrest in the progress of the disease Gowers states that such arrest may be permanent but while this may be a fact it is one that is open to the criticism of incorrect diagnosis since in no other form of the disease has a permanent arrest been recorded The generalized simple atrophic type of the disease is the most rapid especially when it commences with severe initial flaccid paralysis without atrophy There are some exceptions however to this rule for occasionally a commencement with severe non atrophic flaccid palsy is followed by the development of a slowly progressive local type

In the bulbar types of the disease and in amyotrophic lateral sclerosis the course is for the most steadily progressive Every type will show however upon occasion exacerbations and remissions The exacerbations are most important and in the bulbar types may bring about the end in a few hours Of particular interest are rapid extensions of a flaccid paralysis which may occur in a few hours and which resemble and indeed are identical with onset of the disease with initial flaccid paralysis without atrophy which has been already described Whatever type of the disease be present it tends in the end to spread and to become general

Involvement of the respiratory muscles or severe bulbar symptoms and the pulmonary complications which may accompany either condition may bring about the fatal issue It is usual however for death to occur in a manner which is common to so many degenerative nervous diseases where a rapid increase of the paralysis is associated with an increasing lethargy which soon deepens into a rapidly fatal coma It is as if an acute toxic process occurs when the nervous degeneration becomes rapid It is uncommon for death to occur from intercurrent maladies The average tenure of existence after definite signs are present is under one year in the gener

alized flaccid type and it may be as short as two months Bulbar symptoms are not generally survived for more than twelve months Localized cases of simple atrophy may live for many years Those cases in which lead has been a factor are said sometimes to become arrested when the advent of this poison into the system ceases Some of the patients in whom a positive Wassermann reaction is found improve and the disease is sometimes arrested by antisyphilitic treatment

Complications

By far the most common complication which is met with in cases of progressive muscular atrophy is the presence of some syphilitic lesion of the nervous system and this may be of any nature both local and general Tabes dorsalis associated with progressive muscular atrophy is not uncommon It is necessary to carefully exclude from consideration in this place the very commonly occurring cases of tabes dorsalis in which local muscular atrophy occurs for such muscular atrophy does not progress beyond a certain point and it is due to local syphilitic lesions affecting the ventral horn cells or ventral roots General paralysis of the insane has been noted in a few cases as has also paralysis agitans

Diagnosis

The malady has to be distinguished from the many conditions in which progressive weakness and wasting of the muscles occur and again from those in which muscular wasting and spasticity are conspicuous clinical features and lastly from other diseases in which bulbar symptoms are early evidenced In the comparatively rare cases in which spasticity appears before any wasting of muscles is observable an attempt must be made to separate the malady from among the many conditions in which spasticity appears as the earliest sign

Peroneal muscular atrophy very closely resembles progressive muscular atrophy in that slow wasting and fibrillation of the muscles are the chief clinical features The points which distinguish the two conditions are that peroneal atrophy is often a familial disease and it is apt to commence in childhood when it is unusual for progressive muscular atrophy to begin The location of the atrophy is peculiar and when well marked in the periphery of all four limbs as is common in this disease cannot be confused with progressive muscular atrophy since the latter disease never has this distribution Peroneal atrophy never becomes general it does not spread beyond a certain point The atrophy is accompanied by a peculiar hard fibrosis of the muscles and by contractures It is little incapacitating as compared

with progressive muscular atrophy and in some of the cases there is deep loss of sensibility.

Syringomyelia is easily distinguishable by the early and striking loss of pain and temperature sensibility. Cervical rib not uncommonly produces atrophy *of the intrinsic muscles of the hand* and though this is usually confined to one hand it may be bilateral. Pain in the distribution of the eighth cervical and first dorsal roots and some loss of sensibility may be present. The atrophy remains local and is never accompanied by fibrillation. The abnormal rib is easily discoverable on radiographic examination. It must be borne in mind that cervical ribs are not uncommon and that their presence does not necessarily prove the cause of atrophy of the hand muscles, for cervical ribs may be present in progressive muscular atrophy, in syringomyelia and any other disease.

Arthritic muscular atrophy occurs in the regions of inflamed joints which show easily recognizable disease. Fibrillation does not occur, nor are there alterations in the electrical excitability of the wasted muscles. Myotonia congenita is at once separated from progressive muscular atrophy by the myotonus when this latter symptom is present. When myotonus is absent the characteristic wasting of the sternomastoid and of the muscles of the thighs, the age of the subject and sometimes the presence of cataract should suggest the diagnosis.

The muscular dystrophies may be confused with progressive muscular atrophy in cases where familial incidence is absent and when the onset occurs in adult life. Fibrillation never occurs in myopathy. The distribution of the atrophy is in the proximal muscles and trunk muscles first and is peculiar and quite dissimilar from that of progressive muscular atrophy. The disabilities resulting from the muscular dystrophy are peculiarities in gait, in rising from the ground, in attitude and in facial expression so distinct as to render mistake impossible. Articulation is not affected in myopathy and pseudohypertrophy, if present, is pathognomonic. Lesion of peripheral nerve trunks may be diagnosed by the history of a local cause, by the discovery of a palpable local lesion upon the course of the nerve and by the confinement of the atrophy to the distribution of one particular nerve while often pain and sensory loss occur in that same distribution.

Lesions of the nerve roots and especially those produced by pachymeningitis and by neoplasm in the vertebrae may cause signs and symptoms so closely resembling those of the more rapid forms of progressive muscular atrophy as to render correct diagnosis very difficult. Such a lesion in the cervical region, for example, may give rise to wasting of the hand and forearm muscles and a spastic condition of the legs resembling exactly a condition of amyotrophic lateral sclerosis without deformity or rigidity of the spine and without pain or sensory loss. In such cases of difficulty the

course of time will bring the advent of conclusive symptoms of a local pressure lesion It is important in this connection to remember that pressure upon the spinal cord results in hyperalbuminosis of the cerebro spinal fluid and if the lesion causing the pressure is syphilitic there is likely also to be lymphocytosis in that fluid neither of which conditions is found in progressive muscular atrophy Symptoms resembling those of amyo trophic lateral sclerosis may arise from tumor involving the cervical enlarge ment The latter condition becomes easily diagnosable from the not long delayed appearance of sensory loss both upon the arms and upon the trunk below the level of the lesion Fibrillation is never present in any pressure lesion of peripheral nerve nerve root or spinal cord

Multiple neuritis is not usually a source of error in the diagnosis of progressive muscular atrophy since pain and other subjective sensations tenderness sensory loss and trophic changes may be conspicuous In those forms of multiple neuritis however in which the incidence is chiefly or entirely upon the motor structures the clinical picture may closely resemble the acute flaccid palsy without wasting which is sometimes the initial phenomenon to appear in progressive muscular atrophy Fibrillation does not serve to distinguish the conditions for it is not often seen in the initial flaccid palsy of progressive muscular atrophy Further the considerable temporary improvement which may occur after such an onset in progressive muscular atrophy may so resemble that recovery usual in neuritis as to confirm an erroneous diagnosis In such cases the presence of any known cause for multiple neuritis on the one hand and the lapse of time which will bring an augmentation of symptoms and the appearance of fibrillation instead of further recovery upon the other must be relied upon to settle the diagnosis

Tumors of the brain stem and bilateral lesions of the lower pyramidal area and corresponding part of the pyramidal tract may give rise to bulbar symptoms resembling those of progressive muscular atrophy The signs are of the spastic type only Tumors of the brain stem are at once distin guished by the presence of signs of involvement of structures which are never symptomatically affected in progressive muscular atrophy such as the cerebellar tracts the sensory paths and the cranial nerve trunks Spastic bulbar paralysis from lesions of both hemispheres is usually easily separated from the spastic bulbar paralysis of progressive muscular atrophy by the history

Diagnosis is most difficult in those cases where spasticity in the limbs is the first sign of progressive muscular atrophy to appear and where such spasticity precedes the appearance of any muscular atrophy by a long time If it be clearly borne in mind that spastic paralysis may be the earliest and for a time the only sign of progressive muscular atrophy and

that among the many diseases of the nervous system which commence with the same clinical picture of spastic paralysis a certain diagnosis cannot be made until further distinguishing signs appear error will be avoided The importance of the examination of the cerebrospinal fluid in all cases cannot be too strongly emphasized

Prognosis

The progressive character of the disease renders the prognosis grave in every case There are some cases occurring in middle life presumably cases of progressive muscular atrophy of local distribution and slow onset and course which become finally arrested or even improve but in the absence of pathological verification the true nature of such cases is open to doubt Slowly progressive local cases usually last five years and may live as long as twenty five years from the onset In these the malady becomes general in the end The possibility of the occurrence of rapidly advancing generalization always renders the prognosis uncertain

In amyotrophic lateral sclerosis the average duration of life is not more than two years from the onset When bulbar symptoms are present the average duration is under two years In the generalized cases the average duration is under one year Widely spread fibrillation in muscles which are neither weak nor wasted is the constant herald of generalization and renders the immediate prognosis serious In cases where syphilis is present or where lead poisoning is a definite factor the prognosis is more favorable and there is even a possibility of arrest and of improvement if energetic treatment of these associated conditions is provided Rapid extension of the weakness the advent of bulbar symptoms involvement of all the respiratory muscles and especially general asthenia and drowsiness are the signs which usher in the fatal result

Treatment

In most cases this malady seems to be entirely uninfluenced by any treatment that has hitherto been adopted Even where syphilis or lead is a factor in the causation although appropriate treatment for these conditions has been applied and improvement and even arrest may result it is no rare thing to see no amelioration in the rate of progress and in some cases such treatment seems actually to hasten the progress of the disease The value of treatment by the hypodermic injection of strychnin which was claimed by Gowers has not been borne out

It remains therefore to secure favorable conditions of life for the patient and to maintain the general health in as perfect a state as possible Cold

fatigue and traumatic influences such as falls are carefully to be avoided as likely to increase the disability and incite extension of the disease. Absolute rest is not essential and adherence to light occupation where possible seems *to hinder rather than to advance the progress of the disease*.

All tonic remedies are useful. Organotherapy has been largely vaunted but any advantage gained therefrom is from the tonic effect upon metabolism. It has no specific effect upon the malady. Electricity, massage and passive movements are useful as giving bodily comfort to the patient and satisfying him that something is being done for him and that nothing has been left untried. Electricity when strongly applied does harm and faradism must not be used in spastic cases.

In bulbar cases the dysphagia must be aided by avoiding liquids and solids and by serving all the articles of diet in pultaceous form. Salivation which is so troublesome in this condition, may be greatly helped by the administration of hyoscin by the mouth. In the rare cases where sphincter trouble is prominent the regular administration of belladonna is of signal service. In the bedridden state cleanliness and careful attention to the skin and to the regular shifting of the patient will prevent the formation of bedsores. Prevention in the case of bedsores is of the utmost importance for it is far easier to prevent than it is to cure a bedsore.

III

Myotonia Atrophica

Revised by W. Russell Brain

Myotonia atrophica is a very slowly progressive form of muscular atrophy associated with conspicuous slowness in the relaxation of the affected muscles after they have been put into voluntary contraction and of peculiar distribution in that the facial muscles, the muscles of the neck especially the sternomastoids, the muscles of the forearms and hands, the quadriceps femoris and the muscles of the leg below the knee are especially prone to the affection. The disease which commences usually in the third decade of life affects both sexes and may be familial and hereditary. This malady first received special notice from Noques, Sirol and Hoffmann who drew attention to the occurrence of muscular atrophy in cases otherwise resembling Thomsen's disease. Rossolimo separated the condition as a clinical entity in 1902 and applied to it the term myotonia atrophica. Steinert in 1909 first showed that the histological changes in the affected muscles resembled those found in the myopathies and he found some degeneration in the posterior columns of the spinal cord.

Etiology

The limits of age at which the symptoms of this disease have made their appearance in the cases at present recorded have been from fifteen years to forty years but the commencement is much more common between the ages of twenty and thirty years Both sexes are affected but the incidence is more commonly among the males Cases in which no familial relation can be traced are common enough but sometimes several children of the same generation suffer and there is evidence that the malady has been transmitted from one generation to another In such families it is usual for cataract to be the only abnormality for several successive generations in each of which it occurs at an earlier age until in one generation the whole picture of myotonia atrophica becomes manifest

No causal factors have been discovered The slowness of relaxation of the affected muscles after volitional contraction and after both faradic and galvanic excitation resembles the slow relaxation after excitation which is seen in muscles poisoned by veratrin or by sodium phosphate and in lesser degree in muscles which have been fatigued or exposed to cold A general circulatory poison however cannot be responsible for the myotonia in this disease for often the majority of the muscles escape And even the wasted muscles show the myotonia in very unequal degrees For example the forearm muscles and face usually present myotonia conspicuously while the sternomastoids vasti and muscles of the legs though severely wasted may show little or no myotonia Further the wasting of the muscles in a given case may precede the appearance of myotonia for years and vice versa and the myotonia may be most marked in muscles which are not obviously wasted It would therefore seem that there is a double pathological condition present the one a local metabolic disorder within certain muscles which varies in degree from time to time so giving rise to the myotonia which may vary widely in degree from hour to hour and the other a dystrophic disturbance which ends in the atrophy of muscles and that these two pathological conditions are not coincident either as regards time or locality of incidence

Pathology

The histological changes present in the wasted muscles are those which *are found also in the myopathies and in amyotonia congenita and consist* in a sequence of regressive changes in the muscle fibers followed by a secondary interstitial fibrosis with sclerosis of the blood vessels and deposit of fat

fatigue and traumatic influences such as falls are carefully to be avoided as likely to increase the disability and incite extension of the disease Absolute rest is not essential and adherence to light occupation where possible seems to hinder rather than to advance the progress of the disease

All tonic remedies are useful Organotherapy has been largely vaunted but any advantage gained therefrom is from the tonic effect upon metabolism It has no specific effect upon the malady Electricity massage and passive movements are useful as giving bodily comfort to the patient and satisfying him that something is being done for him and that nothing has been left untried Electricity when strongly applied does harm and faradism must not be used in spastic cases

In bulbar cases the dysphagia must be aided by avoiding liquids and solids and by serving all the articles of diet in pultaceous form Salivation which is so troublesome in this condition may be greatly helped by the administration of hyoscin by the mouth In the rare cases where sphincter trouble is prominent the regular administration of belladonna is of signal service In the bedridden state cleanliness and careful attention to the skin and to the regular shifting of the patient will prevent the formation of bedsores Prevention in the case of bedsores is of the utmost importance for it is far easier to prevent than it is to cure a bedsore

III

Myotonia Atrophica

Revised by W RUSSELL BRAIN

Myotonia atrophica is a very slowly progressive form of muscular atrophy associated with conspicuous slowness in the relaxation of the affected muscles after they have been put into voluntary contraction and of peculiar distribution in that the facial muscles the muscles of the neck especially the sternomastoids the muscles of the forearms and hands the quadriceps femoris and the muscles of the leg below the knee are especially prone to the affection The disease which commences usually in the third decade of life affects both sexes and may be familial and hereditary This malady first received special notice from Noques Sirol and Hoffmann who drew attention to the occurrence of muscular atrophy in cases otherwise resembling Thomsen s disease Rossolimo separated the condition as a clinical entity in 1902 and applied to it the term myotonia atrophica Steinert in 1909 first showed that the histological changes in the affected muscles resembled those found in the myopathies and he found some degeneration in the posterior columns of the spinal cord

Etiology

The limits of age at which the symptoms of this disease have made their appearance in the cases at present recorded have been from fifteen years to forty years but the commencement is much more common between the ages of twenty and thirty years Both sexes are affected but the incidence is more commonly among the males Cases in which no familial relation can be traced are common enough but sometimes several children of the same generation suffer and there is evidence that the malady has been transmitted from one generation to another In such families it is usual for cataract to be the only abnormality for several successive generations in each of which it occurs at an earlier age until in one generation the whole picture of myotonia atrophica becomes manifest

No causal factors have been discovered The slowness of relaxation of the affected muscles after volitional contraction and after both faradic and galvanic excitation resembles the slow relaxation after excitation which is seen in muscles poisoned by veratrin or by sodium phosphate and in lesser degree in muscles which have been fatigued or exposed to cold A general circulatory poison however cannot be responsible for the myotonia in this disease for often the majority of the muscles escape And even the wasted muscles show the myotonia in very unequal degrees For example the forearm muscles and face usually present myotonia conspicuously while the sternomastoids vasti and muscles of the legs though severely wasted may show little or no myotonia Further the wasting of the muscles in a given case may precede the appearance of myotonia for years and vice versa and the myotonia may be most marked in muscles which are not obviously wasted It would therefore seem that there is a double pathological condition present the one a local metabolic disorder within certain muscles which varies in degree from time to time so giving rise to the myotonia which may vary widely in degree from hour to hour and the other a dystrophic disturbance which ends in the atrophy of muscles and that these two pathological conditions are not coincident either as regards time or locality of incidence

Pathology

The histological changes present in the wasted muscles are those which are found also in the myopathies and in amyotonia congenita and consist in a sequence of regressive changes in the muscle fibers followed by a secondary interstitial fibrosis with sclerosis of the blood vessels and deposit of fat

Some of the muscle fibers are found to be of abnormally large size with a considerable amount of undifferentiated sarcoplasm As the disease progresses the nuclei of the sarcolemma multiply and invade the substance of the fiber The transverse striation is gradually lost and the giant fiber splits up longitudinally into several smaller fibers which gradually dwindle in size take on a deep stain with hematoxylin and disappear the sarcolemma sheaths alone remaining Apart from the giant fibers the other fibers making up the muscle bundles show the same nuclear proliferation with gradual wasting of the muscle substance and final disappearance the change taking place irregularly fiber by fiber so that normal and degenerate muscle fibers are seen lying together in the same field

Clinical Aspect

The onset is insidious and may be so gradual that the patient himself may be little aware of any disability until instability of the legs and frequent tumbles or incapacity for sustained exertion or his facial appearance call the attention of relatives and bring him under examination In other cases the wasting of the muscles especially of the quadriceps femoris is first noticed and this may precede the development of any disability for many months In other cases again the myotonia and slowness of relaxation and therefore of movement first attract attention

Weakness of the facial muscles with the somewhat blank expression and weak wan smile with inability to close the eyes forcibly and with the prominent lower lip hanging away from the teeth from weakness of the orbicularis oris is characteristic of this malady though the degree of weakness may vary greatly and may be entirely absent The facial aspect when myotonia is marked is most characteristic for when the patient smiles or otherwise puts the facial muscles into forcible contraction the relaxation is very slow and produces an appearance so curious that the disease often may be recognized at once by this sign alone

The sternomastoids usually are conspicuously wasted sometimes to complete disappearance and this constitutes an important sign of the disease This wasting may involve other muscles of the neck and may spread to the scapulo thoracic and humero thoracic muscles giving rise together with the facial weakness to an aspect not unlike that of the facio scapulo humeral form of myopathy The muscles of the pectoral girdle however are never so severely wasted in myotonia atrophica as in myopathy In the upper extremities wasting of the intrinsic muscles of the hand and of the peripheral part of the forearm is characteristic of the malady and it is in the muscles of the forearm and especially in the flexors

that the myotonia is most conspicuous After forcible grasping of the examiner s hand the patient cannot relax for some seconds and to aid the disengagement he pulls his still gripping hand away

The trunk muscles usually are exempt both from the atrophy and the myotonia The quadriceps femoris and especially the vasti are often picked out by early and conspicuous wasting consequently weakness of the legs and diminution or disappearance of the knee jerk are most important signs of the disease and are often those which first call attention The muscles below the knee usually escape Sensibility is normal The sphincters are unaffected Cataract is not uncommonly met with in the subjects of myotonia atrophica Frontal alopecia is the rule and contributes to the characteristic appearance of the patient There is usually atrophy of the gonads leading to impotence in the male and amenorrhea in the female

Prognosis

The course of the malady is very slow and it has no tendency to destroy life though very considerable incapacity may result Some cases are slowly progressive for many years while others seem to come to a standstill and remain without advance of symptoms A few of the cases have improved even to the loss of all symptoms

Diagnosis

The diagnosis is an easy matter in all the cases where the distribution of the atrophy is typical and where myotonia is obvious It simply involves a recognition of the unique characters of this disease In cases where the appearance of the myotonia precedes that of the wasting the age of onset will suggest the diagnosis and the developments of any trace of facial weakness or of muscular wasting will render it certain Much more difficult are those cases in which the myotonia does not appear until long after the muscular wasting is conspicuous Indeed it is impossible to make the diagnosis with certainty until myotonia does appear and the cases are liable to be confused with peroneal atrophy with progressive muscular atrophy and with the facio scapulo humeral form of myopathy Wasting of the quadriceps with diminution or loss of knee jerk should always suggest the possibility of myotonia atrophica as should also the combination of facial weakness and atrophy of sternomastoids The presence of fibrillation in the wasting muscle should exclude myotonia atrophica

Some of the muscle fibers are found to be of abnormally large size with a considerable amount of undifferentiated sarcoplasm As the disease progresses the nuclei of the sarcolemma multiply and invade the substance of the fiber The transverse striation is gradually lost and the giant fiber splits up longitudinally into several smaller fibers which gradually dwindle in size take on a deep stain with hematoxylin and disappear the sarcolemma sheaths alone remaining Apart from the giant fibers the other fibers making up the muscle bundles show the same nuclear proliferation with gradual wasting of the muscle substance and final disappearance, the change taking place irregularly fiber by fiber so that normal and degenerate muscle fibers are seen lying together in the same field

Clinical Aspect

The onset is insidious and may be so gradual that the patient himself may be little aware of any disability until instability of the legs and frequent tumbles or incapacity for sustained exertion or his facial appearance call the attention of relatives and bring him under examination In other cases the wasting of the muscles especially of the quadriceps femoris is first noticed and this may precede the development of any disability for many months In other cases again the myotonia and slowness of relaxation and therefore of movement first attract attention

Weakness of the facial muscles with the somewhat blank expression and weak wan smile with inability to close the eyes forcibly and with the prominent lower lip hanging away from the teeth from weakness of the orbicularis oris *is characteristic of this malady* though the degree of weakness may vary greatly and may be entirely absent The facial aspect when myotonia is marked is most characteristic for when the patient smiles or otherwise puts the facial muscles into forcible contraction the relaxation is very slow and produces an appearance so curious that the disease often may be recognized at once by this sign alone

The sternomastoids usually are conspicuously wasted sometimes to complete disappearance and this constitutes an important sign of the disease This wasting may involve other muscles of the neck and may spread to the scapulo thoracic and humero thoracic muscles giving rise together with the facial weakness to an aspect not unlike that of the facio scapulo humeral form of myopathy The muscles of the pectoral girdle however are never so severely wasted in myotonia atrophica as in myopathy In the upper extremities wasting of the intrinsic muscles of the hand and of the peripheral part of the forearm is characteristic of the malady and it is in the muscles of the forearm and especially in the flexors

that the myotonia is most conspicuous After forcible grasping of the examiner s hand the patient cannot relax for some seconds and to aid the disengagement he pulls his still gripping hand away

The trunk muscles usually are exempt both from the atrophy and the myotonia The quadriceps femoris and e pecially the vasti are often picked out by early and conspicuous wasting consequently weakness of the legs and diminution or disappearance of the knee jerk are most impor tant signs of the disease and are often those which first call attention The muscles below the knee usually escape Sensibility is normal The sphincters are unaffected Cataract is not uncommonly met with in the subjects of myotonia atrophica Frontal alopecia is the rule and con tributes to the characteristic appearance of the patient There is usually atrophy of the gonads leading to impotence in the male and amenorrhea in the female

Prognosis

The course of the malady is very slow and it has no tendency to de stroy life though very considerable incapacity may result Some cases are slowly progressive for many years while others seem to come to a stand still and remain without advance of symptoms A few of the cases have improved even to the loss of all symptoms

Diagnosis

The diagnosis is an easy matter in all the cases where the distribution of the atrophy is typical and where myotonia is obvious It simply in volves a recognition of the unique characters of this disease In cases where the appearance of the myotonia precedes that of the wasting the age of onset will suggest the diagnosis and the developments of any trace of facial weakness or of muscular wasting will render it certain Much more difficult are those case in which the myotonia does not appear until long after the muscular wasting is conspicuous Indeed it is impossible to make the diagnosis with certainty until myotonia does appear and the cases are liable to be confused with peroneal atrophy with progressive muscular atrophy and with the facio scapulo humeral form of myopathy Wasting of the quadriceps with diminution or loss of knee jerk should always suggest the possibility of myotonia atrophica as should also the combination of facial weakness and atrophy of sternomastoids The pres ence of fibrillation in the wasting muscle should exclude myotonia atroph ica

The importance of examining the patient on frequent occasions must be insisted upon because the myotonia which is the all important physical sign, is variable In the same case it may be now present now absent at one hour well marked and at another little marked Repeated effort will as a rule increase it

Treatment

There is no curative treatment for this disease Attention to the general health and to the well being of the patient in providing such occupation as his capacity will allow while avoiding fatigue or cold and especially long confinement to bed are the measures which are most likely to help There is no evidence that either electrical treatment or massage has any effect in altering the course of the disease It has recently been found that quinine in doses of 0 3 gm (5 grains) of the hydrochloride two or three times a day may abolish the myotonia

IV

Progressive Spinal Muscular Atrophy of Children

The Werdnig-Hoffmann Disease

Revised by W RUSSELL BRAIN

This is a malady of the first year of infancy often incident upon several children of the same parents and characterized by the gradual development of progressive muscular weakness and atrophy which affects the proximal muscles first and most increases to a complete paralysis of trunk and limbs and finally affects the bulbar muscles The disease is invariably fatal in from a few weeks to several months The most striking pathological changes are a progressive degeneration and disappearance of the ventral horn cells of the spinal cord and of their homologues in the brain stem

Etiology

In some of the cases the paralysis is noticeable at the time of birth and the disease is obviously of prenatal development In others the children are quite healthy at birth and the disease develops some time during the first year of life and most frequently within eight weeks of birth Though sporadic cases may be met with yet in the majority of instances several

children of the same mother are affected Both the prenatal cases and the postnatal cases may be met with among the children of the same mother Thus in one family the mother had eight children Of these the third fifth sixth and seventh were perfectly healthy at the age of puberty In the first child the paralysis was noticed at four weeks old and the child died at five months In the second the malady appeared at the sixth month and death occurred at the eighth month In the fourth child the onset was at six weeks old and death occurred at the seventh month In the eighth child paralysis was marked at the time of birth and death occurred in the eighth week Diagnosis was confirmed by pathological examination in three of these cases The sexes seem to be equally affected No maternal ill health during pregnancy has been noticed and nothing is known about any other etiological factor

Morbid Anatomy

The most extensive changes are found in the ventral horn cells throughout the spinal cord and brain stem and at many levels no normal cells whatever are to be seen Tigrolysis swelling and glassiness of the cells extrusion of the nuclei disappearance of the dendrites shrinking of the cells and final disappearance is the sequence of the changes Degeneration of the anterior roots and of the peripheral motor nerve fibers consequently occurs These changes are not confined to the lower motor neurons for examination by the Marchi method shows extensive degeneration throughout the posterior columns of the cord indicating that lower sensory neurons were also considerably affected

The muscles show intense degeneration with hypertrophy of a few fibers and atrophy of most of the fibers waving moniliform shape hypernucleation of the spindles general nuclear increase and fibrosis are other changes that are seen

Clinical Aspect

In the cases which are prenatal the malady is noticed at the time of birth on account of the tonelessness and flaccidity and the poorness of movement in the trunk and proximal muscles of the limbs In the postnatal cases there is a gradual onset of similar weakness and flaccidity in the trunk first and in the limbs afterwards, which usually commences within six weeks of birth but which may not appear until towards the end of the first year of life The weakness seems always to be least marked in the periphery of the limbs where curious slow involuntary

movements of the fingers and toes have been noted in a good many of the cases The paralysis is followed by a rapid and extensive wasting of the muscles accompanied by occasional fibrillary twitchings Since these children are not only well nourished but often put on much fat during the illness the wasting of the muscles may not be apparent on inspection or palpation It can however be detected immediately by radiography which distinguishes sharply between fat and muscle

As the malady progresses the trunk muscles become completely paralyzed the intercostal muscles being always paralyzed before the diaphragm is affected The limbs become progressively weaker and lastly bulbar paralysis supervenes in those cases where death has not already occurred from respiratory paralysis The reaction of degeneration is present in the affected muscles Sensibility may be unimpaired but in several of my cases there has been conspicuous loss of pain sensibility over the limbs and trunk The sphincters are unimpaired until the very last stages of the disease The superficial and deep reflexes are lost The ocular muscles have not been affected and intelligence is preserved throughout the course of the disease

Course and Prognosis

The course invariably is progressive and is more rapid the earlier in life the disease commences It is most rapid of all in the prenatal cases which usually are fatal within a few weeks With an onset some weeks after birth life usually is continued for several months and a few cases have been reported in the literature with an onset towards the end of the first year and in these death has been delayed not taking place until the third or fourth year

Diagnosis and Treatment

The peculiar and striking features of the disease make the diagnosis easy if the symptomatology be known Amyotonia congenita presents the same helplessness and flaccidity of trunk and limbs as does the Werdnig Hoffmann disease and further resembles it in being sometimes congenital and sometimes having an onset very early in life In amyotonia congenita however the paralysis is not complete and it tends to improvement and not to progressive increase Contractures also occur which are not found in the Werdnig Hoffmann disease and lastly the definite spinal cord changes of the latter malady are not found in the former No treatment is known to influence the course of the malady

V

Subacute Combined Degeneration

Revised by W Russell Brain

Synonyms — The anemic spinal disease (Nonne) funicular myelitis (Henneberg)

Subacute combined degeneration is a disease most common in the second half of adult life The lesions of the nervous system are unlike those occurring in any other disease in that no neuroglial increase follows the degeneration The posterior and lateral columns of the spinal cord are early affected and it is to the affection of both these columns that the term combined degeneration alludes The clinical features are usually strikingly distinct in that subjective sensations such as tingling numbness and burning occurring usually at the periphery of the limbs are early obtrusive and persistent symptoms and are accompanied or followed by the development of a paraplegia which may be of a spastic type or of a flaccid and ataxic type or of a mixed type according to the degree of affection of the lateral and of the posterior columns and of the peripheral nerves

The deep reflexes are present exaggerated or absent according to the relative affection of these structures The superficial reflexes are remarkably brisk in sharp contrast to the diminution of these reflexes which usually obtains when the lateral columns of the cord are affected Loss of sensibility of peculiar distribution occurs which has a glove and stocking distribution upon the limbs and a segmental distribution upon the trunk In the late stages of the malady the paraplegia tends to become complete and of the flaccid type with loss of the deep reflexes Anemia of the megalocytic Addisonian or pernicious type is usually but not invariably present

Etiology

First met with in the third decade of life the malady becomes increasingly frequent until a maximum incidence occurs in the sixth decade while cases commencing in the seventh decade are not uncommon Among 128 cases occurring at the National Hospital London the earliest commencement occurred at 26 years Four cases commenced before the thirtieth year Twenty two cases commenced in the decade 30 to 40 years thirty three in the decade 40 to 50 years fifty two in the decade 50 to 60

movements of the fingers and toes have been noted in a good many of the cases The paralysis is followed by a rapid and extensive wasting of the muscles accompanied by occasional fibrillary twitchings Since these children are not only well nourished but often put on much fat during the illness the wasting of the muscles may not be apparent on inspection or palpation It can however be detected immediately by radiography which distinguishes sharply between fat and muscle

As the malady progresses the trunk muscles become completely paralyzed the intercostal muscles being always paralyzed before the diaphragm is affected The limbs become progressively weaker and lastly bulbar paralysis supervenes in those cases where death has not already occurred from respiratory paralysis The reaction of degeneration is present in the affected muscles Sensibility may be unimpaired but in several of my cases there has been conspicuous loss of pain sensibility over the limbs and trunk The sphincters are unimpaired until the very last stages of the disease The superficial and deep reflexes are lost The ocular muscles have not been affected and intelligence is preserved throughout the course of the disease

Course and Prognosis

The course invariably is progressive and is more rapid the earlier in life the disease commences It is most rapid of all in the prenatal cases which usually are fatal within a few weeks With an onset some weeks after birth life usually is continued for several months and a few cases have been reported in the literature with an onset towards the end of the first year and in these death has been delayed not taking place until the third or fourth year

Diagnosis and Treatment

The peculiar and striking features of the disease make the diagnosis easy if the symptomatology be known Amyotonia congenita presents the same helplessness and flaccidity of trunk and limbs as does the Werdnig Hoffmann disease and further resembles it in being sometimes congenital and sometimes having an onset very early in life In amyotonia congenita however the paralysis is not complete and it tends to improvement and not to progressive increase Contractures also occur which are not found in the Werdnig Hoffmann disease and lastly the definite spinal cord changes of the latter malady are not found in the former No treatment is known to influence the course of the malady

Morbid Anatomy

The essential lesion is confined to the white matter of the spinal cord and brain stem The gray matter is unaffected except for the changes which result from destruction of certain tracts in the white matter and the changes which occur from the profound metabolic disorder which is present when the malady is far advanced Such changes are often conspicuous in the Betz cells of the ascending frontal convolution in Purkinje s cells of the cerebellum and in the cells of Clarke s column as Gordon Holmes has pointed out The meninges and the anterior and posterior roots are normal but some degeneration is always found in the peripheral nerves In macroscopic appearance the spinal cord is larger than normal since the nature of the lesion is edematous and there is no neuroglial condensation and in this respect the disease differs widely from other forms of posterolateral and scattered degeneration for in these latter conditions shrinking of the spinal cord is always conspicuous

The degeneration usually commences in the lower dorsal region of the cord and is first seen in the center of both posterior columns and soon afterwards in the center of either lateral column as small areas of a darker and more translucent appearance than the normal white matter (Fig 2) It is only at an early stage of the disease that the anatomical picture is strictly one of posterolateral degeneration for soon after spots of degeneration appear on either side of the anterior median fissure and in other parts of the anterolateral columns (Fig 3) The degenerate areas increase in size centrifugally coalesce with one another reach the surface of the cord and eventually involve the whole of the white matter of the cord as seen in transverse section with the exception of the narrow zone of short internuncial fibers which everywhere clothes the gray matter (Fig 4) This annular or ferrule like degeneration in the lower dorsal region is highly characteristic and occurs in no other disease

From its starting point in the lower dorsal region the degeneration spreads upwards and downwards in the white columns of the spinal cord and for this reason the term funicular myelitis was applied to it by Henneberg This extension depends upon the occurrence of small isolated spots of degeneration in the posterior lateral and anterolateral columns which increase in size and thus join the area previously degenerated While in its earlier stages the degeneration is confined to definite regions of the white matter it does not resemble a system disease of the spinal cord as it advances by the formation and coalescence of separate small focal lesions

The degeneration tends to extend upwards indefinitely and in severe

years and seventeen in the decade 60 to 70 years The latest commencement was at the age of 69 years The sexes are equally affected

The familial occurrence of subacute combined degeneration is rare but it is well authenticated that multiple cases of this disorder and pernicious anemia may occur in the same family and sometimes in several generations

At one time it was believed that the degeneration of the nervous system was secondary to the anemia but that this view is incorrect is shown by the occasional occurrence of subacute combined degeneration in the absence of anemia and by the fact that the nervous disorder may progress though the anemia has been arrested by treatment

The work of Minot and Murphy Castle and others has shown that pernicious anemia is due to a deficiency of two factors an intrinsic factor present in normal gastric juice and an extrinsic factor contained in the food possibly vitamin B These two factors apparently combine to form a substance necessary for normal hemopoiesis Sufferers from pernicious anemia have gastric achylia usually as a congenital abnormality and so lack the necessary intrinsic factor

Gildea Kattwinkel and Castle have shown that degeneration of the white matter of the spinal cord can be produced in dogs by chronic deficiency of the antineuritic portion of vitamin B in the diet and Strauss and Castle have suggested the subacute combined degeneration may be due to a combined deficiency of the intrinsic gastric factor and vitamin B_1

Such a hypothesis does not exclude the older view that bacterial or other toxins may play a part in etiology since it is known that both a toxin and a vitamin deficiency may be required to produce degeneration of the spinal cord e g in ergotism

Although subacute combined degeneration usually is associated with anemia of the megalocytic or pernicious type this is not always of the idiopathic or Addisonian variety but the causal condition of both may be partial gastrectomy or gastroenterostomy malignant disease or sprue Rarely the anemia is of the microcytic variety and sometimes anemia is absent Very rarely Hodgkin s disease or leukemia may be associated with subacute combined degeneration in cases in which the absence of lymphogranulomatosis or leukemic deposits in or around the spinal cord has been verified at autopsy

Both pathologically and etiologically there are points of resemblance between the lesions of subacute combined degeneration and those found in the nervous system in ergotism lathyrism and pellagra although they seem quite distinctly different diseases

lesions The destruction of the axons by the local lesions also causes a series of retrograde changes in the corresponding nerve cells and tigrolysis vacuolation shrinking and neurophagy may be conspicuous especially in the cells of Clarke s column and in the cells of Betz which give origin to

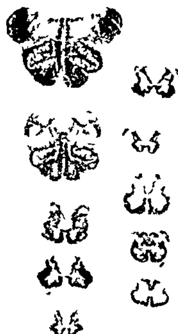


FIG 4 —Sections of the spinal cord and medulla from a long standing case of subacute combined degeneration stained by the Weigert Pal method showing the ferrule like degeneration of all the white matter except the short internuncial fibers surrounding the gray matter in the cervical and dorsal regions The degenerated areas and the gray matter are unstained From a photograph by Dr Greenfield

the pyramidal fibers Acute and widely spread changes in the nerve cells generally may be found and these are in all probability due to a terminal toxemia Kattwinkle considers that the primary spots of degeneration are determined by the vascular distribution and that they result from disease of the perivascular lymphatics In the development of these spots

and advanced cases has been found as high as the internal capsule in the pyramidal tract

The lesions of the white columns entail the usual secondary degenera



FIG 2 —Sections of the spinal cord from a case of subacute combined degeneration with pernicious anemia in which the degeneration is confined to the posterior columns stained by the Weigert Pal method The upper left section shows a recent hemorrhage in the posterior column The symmetrical pale areas in the anterior columns of the upper two right sections represent Helweg s triangular areas and are not areas of degeneration Clinically the case was of the flaccid type with absent deep reflexes and flexor responses throughout From a photograph by Dr Greenfield

FIG 3 —Sections of the spinal cord from a case of subacute combined degeneration before the degeneration has advanced beyond the posterior and lateral regions The commencement of degeneration in the anterior columns in the dorsal region is well shown as a number of minute white points in the second section from the top From a photograph by Dr Greenfield

tions both ascending and descending but these occur late and are often much less obvious than might be expected from the severity of the local

paralysis with loss of the deep reflexes This change from the spastic to the flaccid condition may take place at any stage of the disease All forms of paraplegia are accompanied by marked ataxia Girdle sensations lightning pains fixed pains gastric crises exaggeration of superficial reflexes all are encountered Sphincter paralysis is late Loss of sexual power is early There are muscular wasting and lowering of electrical excitability of general distribution in the paraplegic region

Anemia which may be absent throughout or may become apparent at any period in the course of the disease is conspicuous at the time of the onset of the nervous symptoms in about one half of all cases

Peripheral subjective sensations are so constantly the earliest symptom so discomforting to the patient and so persistent as to form a most distinctive feature of the disease These sensations are variously described but tingling and numbness are the most common Creeping sensations smarting burning icy coldness tightness and pain are all common These sensations usually are felt first upon the tips of the fingers and toes and subsequently spread up the limbs Occasionally they are first noticed in the perineum in the back of the neck and behind the ears and in the tongue Lightning pains indistinguishable from those of tabes occur in many of the cases A girdle sensation is the rule and it is sometimes painful

Sensory loss (Fig 5) commences at the periphery and is distributed in glove and stocking fashion It extends on to the trunk as time goes on and there seems limited by intersegmental lines The muscle sense and sense of position are among the earliest of the sensory perceptions to disappear Generally speaking sensibility to pain and temperature are lost earlier and to a greater extent than is sensibility to touch and as the sensory loss spreads up the trunk the loss to pain precedes the loss to touch In other cases however the tactile loss may precede and exceed the loss to pain and in rare instances tactile and thermal perception have persisted where perception of pain has disappeared In the late stages of long standing cases the sensory loss is likely to become absolute to all forms

The paraplegic signs usually follow the appearance of the subjective sensations but they may be the first evidence of the disease They appear most often insidiously but sometimes rapidly The patient first notices that the legs are easily tired that he drags the feet in walking or that he walks unsteadily in the dark or that he falls forward into the basin when washing himself Slight rigidity of the lower extremities with weakness especially of the dorsiflexors of ankles and toes will be found present with increase of the knee jerks ankle jerks foot clonus a tendency to pes cavus and an extensor type of plantar reflex The defects of coordination are

the following sequence of changes can be seen The earliest is swelling of the medullary sheaths over a small area of the white matter The swollen sheaths then break up by fatty degeneration and the axis cylinders become no longer recognizable The degenerate contents of the swollen medullary sheaths now gradually disappear leaving nothing but the fine connective tissue of the spinal cord surrounding vacuolated spaces of varying size filled with fluid some of which represent the spaces originally occupied by the nerve fibers but others are formed by the fusion of several such spaces However long standing the case may have been there is practically no neurogliar reaction with condensation or shrinkage of the spinal cord and consequently the spinal cord remains large This complete absence of neurogliar proliferation was first pointed out by Long and it distinguishes the lesion of this disease from all other conditions of degeneration within the nervous system

Occasionally the disease is entirely confined to the posterior columns of the spinal cord The peripheral nerves may show considerable degeneration The muscles are conspicuously wasted in the later stages and the muscle fibers show great diminution in size and poor striation There is not any considerable increase of the muscle nuclei and little or no fibrosis occurs

In the majority of cases the pathological changes of pernicious anemia are also present These include anemia glossitis hyperplasia of the red marrow of the long bones slight or moderate enlargement of the spleen and the presence of iron in the reticulo endothelial system

Clinical Aspect

In a large majority of instances the symptoms appear insidiously and without any exciting cause Sometimes the onset is more rapid and may be preceded by severe gastrointestinal symptoms such as vomiting diarrhea jaundice malaise and pyrexia In a few cases the onset has been so rapid as to suggest the diagnosis of acute myelitis

The cardinal signs may be summarized as follows peripheral subjective sensations which occur early and are remarkably obtrusive are complained of in the periphery of the limbs in most cases but may occur in the perineum neck and back of the head and in the tongue Sensory loss is found which commences upon the limbs with peripheral stocking and glove distribution and reaching on to the trunk ascends in segmental distribution Astereognosis occurs in the upper extremities Paraplegia may be (*a*) flaccid from the first with loss of deep reflexes (*b*) spastic remaining spastic throughout (rare) (*c*) spastic changing to flaccid

shown by the loss of sense of passive movement and of position by ataxy of movement and by Romberg s sign

Some cases however form an exception to the rule that spastic ataxy is a characteristic feature of the early stages of the disease for the knee jerk is diminished or lost early and the clinical picture is one of ataxy with flaccid weakness throughout Implication of the lateral column of the spinal cord is shown in such flaccid cases by the presence of the extensor type of plantar reflex This type of case is especially rapid in course Buzzard has reported cases in which the knee jerk returned and became excessive after an initial loss and this is explained by an initial affection of the peripheral nerves and a subsequent affection of the lateral columns

Very rarely the disease is confined to the posterior columns and when this is the case there are no signs of involvement of the pyramidal tract

As the disease advances the paraplegia involves more and more of the trunk progressing upwards In some cases the upper extremities are affected early and may even be the first regions to show signs of the disease In the course of time the paraplegia becomes complete with great wasting of the muscles and reduction of their faradic excitability and when this occurs it is usual for the spasticity to disappear with the onset of a flaccid paraplegia with diminished and finally absent knee jerks the extensor plantar response and the superficial reflexes persisting On the other hand the spastic state sometimes persists to the end in spite of absolute paraplegia and total sensory loss of months duration and in such cases reflex flexor spasms are likely to be a most troublesome feature

The paraplegia does not as a rule reach the upper limits of the region supplied by the cervical enlargement of the spinal cord and even in the most severe cases the condition of the upper extremities is one of partial paralysis most marked in the periphery and associated with considerable wasting of the muscles of the hands and forearms The faradic excitability of the muscles is much reduced and it is diminished in proportion to the wasting In addition to the muscular wasting usually there is conspicuous wasting of the subcutaneous fat In late stages of the disease the general bodily wasting becomes extreme

Loss of sexual power in the male often is an early symptom Dysuria generally appears when the paraplegia becomes pronounced It does not often occur in the early stages of the malady and sometimes its appearance is delayed until remarkably late Finally the control of the rectum and bladder becomes completely lost

Superficial Reflexes — The persistence of a high degree of reflex excita

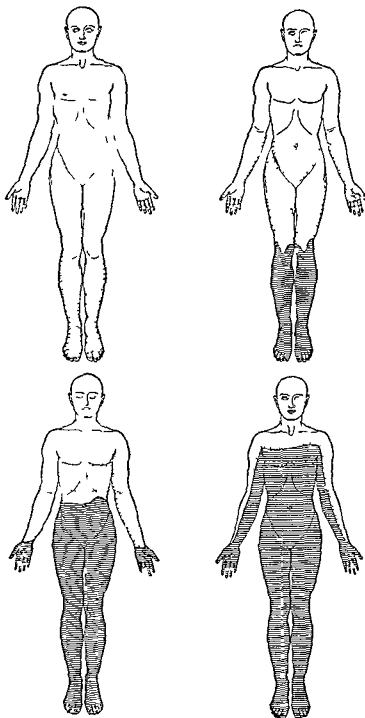


Fig. 5.—Charts of the sensory loss from a case of subacute combined degeneration showing the progressive loss as the disease advances. The dotted areas represent partial loss to pain and to temperature; the lined areas represent complete loss to pain and to temperature with partial loss to touch. The first chart shows the sensory loss three months after the commencement of symptoms; the last chart was taken a few days before the fatal event nine months later. The third chart shows a slight temporary improvement in the sensory loss of the right arm.

cases Small retinal hemorrhages are not uncommon A minor degree of nystagmus is the rule and may depend upon the involvement of the cervical spinal cord all lesions of which seem to be regularly associated with nystagmus or this may be attributed to affection of the cerebellum for changes in the Purkinje cells of this organ have been repeatedly found

The pupils may be small irregular unequal and react poorly to light and there may be narrowing of one or both palpebral apertures and sometimes marked enophthalmos all these signs resulting from interference with the sympathetic mechanism in the lower cervical region of the cord Reflex iridoplegia has been found even where syphilis could be excluded Diplopia occurs occasionally Parasthesia of the fifth nerve distribution has been reported Other bulbar and cerebellar symptoms are occasionally present

Herpes is not infrequent It may occur anywhere and has several times affected the distribution of the trigeminal nerve The cerebrospinal fluid is normal

Although anemia is one of the most characteristic features of subacute combined degeneration since it is sufficiently striking as at once to suggest the diagnosis in at least two thirds of all the patients when they first come under observation for nervous symptoms yet it may be absent throughout the course of the disease and its appearance may be delayed until several years after the disease of the nervous system is manifest

The anemia in almost every case is identical in every respect with pernicious anemia and is characterized by a high color index — 1 to 1 [illegible] or even higher — poikilocytosis anisocytosis and polychromatophilia and the presence of normoblasts and megaloblasts while the white cells show a reduction in number leucopenia with a relative lymphocytosis Even when the red cell count is apparently normal it may be possible by using the Price Jones or other appropriate technique to demonstrate the presence of an excessive number of the large red cells characteristic of pernicious anemia

Gastric achlorhydria is almost invariably present The tongue often exhibits glossitis painful fissures appearing at the margins while the surface becomes smooth and glazed owing to loss of the papillæ Glossitis appears to be more closely related to the anemia than to the nervous disorder Oral sepsis is almost invariably present The skin is typically lemon tinted or biscuit colored The spleen is only occasionally palpable Gastrointestinal symptoms are common especially anorexia flatulence and diarrhea The symptoms and signs common to all anemic states breathlessness headache cardiac and venous murmurs and edema are

bility from the skin of the limbs and trunk even sometimes in the last stages of the malady is remarkable and contrasts strongly with the general lowering or loss of the skin reflexes which obtains in other conditions of paraplegia where the pyramidal tract is involved This easy excitability of the skin reflexes is highly characteristic of the disease The plantar reflexes are flexor at first in about 50 per cent of cases but later become extensor in all but a small proportion In a few cases in which the degeneration is confined to the posterior columns the plantar reflexes remain flexor throughout

Deep Reflexes —These may be increased and may persist in active state until the end In more than 50 per cent of cases the ankle jerks are lost when the patient is first seen rather less often the knee jerks are also lost In rare cases both may be absent at first and subsequently reappear and become brisk The reasons for this variability in the deep reflexes in different cases is not difficult to understand The lesion in the peripheral nerves tends to abolish the deep reflexes and if these are early and severely affected the deep reflexes will be diminished or absent The lesion in the lateral columns often causes exaggeration of the deep reflexes in greater degree than the diminution caused by the peripheral nerve lesion so that with lesions of both these structures the deep reflexes are still exaggerated When the degeneration destroys all the long white columns of the spinal cord the deep reflexes are lost as in total transverse lesion of the cord and the change from the spastic to the flaccid state with loss of the previously exaggerated deep reflexes occurs when all the long white columns are involved The reappearance of the deep reflexes at first absent means that the lesion first involved the peripheral nerves and subsequently attacked the lateral columns

Trophic changes in the nails and skin vasomotor disturbances in the periphery of the limbs and bedsores are of common occurrence Soft translucent edema of the extremities and trunk is frequent especially when the anemia is severe and is dependent upon the anemia and upon the impaired innervation of the paraplegic region

Disorders of mood impairment of memory confusional and depressive states are not uncommon and may occur early General mental deterioration mild delirium drowsiness and torpor frequently occur in the later stages of the disease and are referable to the anemia and also to widely spread cell changes in the cerebrum General convulsions have been reported in a few cases

Dimness of vision is common when anemia and debility are severe Optic neuritis of slight degree is sometimes met with and is doubtless in relation to the anemia Optic atrophy has been reported in a good many

and sensory loss over the trunk however are not found in polyneuritis while pain in the extremities tenderness of the calves wrist drop and foot drop are common in polyneuritis and rare in subacute combined degeneration

In the well developed stages of the disease its recognition presents no great difficulty Attention is quickly attracted by the conspicuous anemia and biscuit colored skin Following a period of slight paraplegia often lengthy the steadily increasing paralysis of the lower extremities with perhaps sudden exacerbations producing complete and lasting helplessness the characteristic distribution of the sensory loss which spreads upwards towards the cervical region the severe lightning pains the irregular pyrexia the anemia and the relatively late onset of sphincter trouble serve to separate this disease from other forms of paraplegia The change from the spastic to the flaccid type of paraplegia with loss of the deep reflexes and persistence of the extensor response which occurs in many of the cases in the late stages is highly characteristic

The distinction from the following diseases which are grouped together as conditions of posterolateral degeneration does not as a rule present much difficulty (1) Friedreich s disease and other forms of hereditary ataxy (2) tabes dorsalis with pyramidal degeneration (3) amyotrophic lateral sclerosis with posterior column degeneration and (4) other forms of systemic combined sclerosis The symptomatology of most of these conditions departs so widely from that of the disea e under consideration as to leave little possibility of confusion The forms of tabes with pyramidal degeneration however require very careful differentiation as so many clinical features are common to the two diseases The peculiar distribution of the pain sensory loss in tabes the manner of advent and the general grouping of the symptoms and signs and the positive Wassermann reactions in blood and cerebrospinal fluid and the presence of lymphocytosis in the latter fluid usually will serve to prevent error

Prognosis

Before the introduction of treatment with liver and liver extract subacute combined degeneration was always fatal usually within two or three years of the appearance of the first symptoms To day it may be claimed that a patient who has pernicious anemia may be prevented from ever developing subacute combined degeneration if given an adequate dose of liver extract When subacute combined degeneration has already developed the degree of improvement which is possible in response to treatment depends upon both the site and the extent of the degeneration Since the

commonly present, but hemorrhages are uncommon Syncopal attacks may occur

Irregular pyrexia is almost invariably present at some period in the course of the disease and this quite apart from fever producing complications such as cystitis and bedsores

Many of the patients are poorly nourished and cachectic at the onset but others are well nourished and may even put on weight in the early stages of the disease as in pernicious anemia In the later stages progressive emaciation is constant

Diagnosis

In the earliest stage and before the appearance of any definite sign of organic spinal disease there may be such disability as to suggest the diagnosis of functional paraplegia This statement is true of many organic diseases of the spinal cord and especially of disseminate sclerosis and spinal tumor When organic signs appear it is especially from disseminate sclerosis spinal tumor tabes dorsalis and polyneuritis that the diagnosis has to be made The preponderance of the peripheral subjective sensations and the presence of a florid complexion with anemia should always suggest the diagnosis Slight spastic ataxy is the common clinical picture of subacute combined degeneration of disseminate sclerosis and of spinal tumor Symmetrical peripheral sensations and peripheral numbness are not features of disseminate sclerosis and the presence of peripheral sensory loss should always challenge that diagnosis whereas diplopia nystagmus transient amblyopia and intention tremor are not early symptoms of subacute combined degeneration Spinal tumor is especially distinguished by a sharp line of sensory loss, transverse to the axis of the body, which does not spread up from below in slow fashion

When the subacute combined degeneration commences with flaccid ataxy and loss of the deep reflexes the distinction must be made from tabes dorsalis The extensor plantar reflex which is almost always present in the former disease and which is rare in early tabes the entirely different distribution of the sensory loss in the two diseases the loss of power in subacute combined degeneration and the results of the examination of the blood and cerebrospinal fluid for syphilitic reactions and of the latter fluid for lymphocytosis are important aids in the differential diagnosis

Since peripheral nerve degeneration usually is present in subacute combined degeneration this condition possesses certain symptoms in common with polyneuritis namely anesthesia of the glove and stocking distribution and loss of the tendon reflexes Extensor plantar responses

In advanced cases the usual care of the skin bladder, rectum and paralyzed limbs necessitated by paraplegia will be required

Foci of sepsis especially in the teeth should receive attention Al though gastric achlorhydria is present the administration of acid is not essential but dyspeptic symptoms may be relieved by giving 1 dr of dilute hydrochloric acid flavoured with syrup of lemon in 6 ounces of water with meals three times a day

VI

Acute Poliomyelitis

Revised by W Russell Brain

Synonyms — Acute infantile paralysis the Heine Medin disease

Acute poliomyelitis (see also Vol V Chap V) an acute specific infec tious febrile disease occurring sporadically and sometimes epidemically is incident chiefly upon young children though no age is exempt It is due to the infection of the respiratory passages with a filterable virus which when injected into monkeys reproduces the disease and can again be recovered from the diseased nervous tissue of the infected animals The clinical aspect of the malady is that of an acute febrile illness of short duration accompanied or followed by severe nervous symptoms indicative of damage to the gray matter of the spinal cord or brain stem The lesion of the spinal cord produces acute atrophic paralysis (infantile atrophic palsy) that of the brain stem produces paralysis of cranial nerves and nuclei (most commonly ophthalmoplegia)

It is probable that the disease frequently occurs without nervous man ifestations as a short febrile illness with complete recovery Carriers of the disease who do not themselves suffer but from whose respiratory passages the organism of the disease can be recovered are probably com mon and these are important agents in the propagation of the disease

Etiology

A most constant feature of the disease is its incidence in young chil dren During the first year of life children seem almost immune but dur ing the second and third year they are most often affected As age advances after the third year the incidence rapidly declines and while cases occurring in early adult life are common enough the disease becomes very uncommon after middle life It would appear that the immunity during

peripheral nerves are capable of regeneration a striking improvement may be expected in the polyneuritic symptoms leading to disappearance of paresthesiæ and pains in the limbs sensory loss of the glove and stocking distribution and muscular wasting with return of tendon reflexes and improvement in muscular coordination Since the nerve fibers of the spinal cord are incapable of regeneration little change can be expected in symptoms due to degeneration of the pyramidal tracts and posterior columns except in the case of a few fibers in which the degenerative change has not gone so far as to be irreversible Extensor plantar responses and spastic weakness of the lower limbs therefore usually persist unchanged

Even in patients in whom the disease has been arrested by treatment the development of an infection especially localized suppuration may lead to a severe and even fatal exacerbation

Treatment

The essential factor the lack of which causes subacute combined degeneration may be administered to the patient either by (1) the mouth in the form of raw or lightly cooked liver liver extract or dessicated hog's stomach or (2) intramuscularly or (3) intravenously in the form of liver extract In most cases the intramuscular injection of liver extract is the method to be preferred since it is relatively cheap and more convenient to the patient as it permits of the formation of a depot in the patient's body and thus reduces both the amount and the frequency of the administration Since liver extracts are prepared by different methods the dosage of different preparations are not equivalent Consequently the dosage to be used must be determined on the basis of the potency of the preparation used Already standardization of potency of liver preparations is being developed and adopted This already has been done by the U S Pharmacopœia Commission If liver is given by the mouth about half a pound of raw or lightly cooked liver is required daily as a maintenance dose or an equivalent amount of liver extract may be used In some cases dessicated hog's stomach seems to be more effective than liver or liver extract and this is given in divided doses amounting to a total of 30 gm a day at first the maintenance dose being somewhat smaller The intramuscular method of administration of liver extract is being widely adopted in the United States For further discussion of liver therapy see Vol II Chap XVI

The recovery of power and coordination in the limbs may be hastened by massage passive movements and reeducational exercises Pains are relieved by such analgesics as aspirin antipyrin (phenazone) etc

bodies but it is now recognized that the microorganism is invisible Since it is capable of passing through a Berkefeld filter it is described as a filterable virus On inoculation the organism reproduces the experimental disease in monkeys Infection either by means of the virus obtained from an infected spinal cord or from the nervous system of monkeys infected experimentally is most easily produced by direct injection into the brain but injections into the peritoneal cavity the anterior chamber of the eye the subcutaneous tissue the intrathecal space and the nerve trunks have all been successful in producing the disease with varying degrees of certainty Injection into the blood nearly always fails as the blood seems to have a definite destroying influence upon the organisms It has been shown that the disease can be communicated to monkeys by applying the virus to the uninjured nasal or intestinal mucous membrane In living patients during the acute stage of the disease and in those who have died of the disease the presence of the microbe has been detected in the secretions of the mucous membranes of either the mouth the nose the upper air passages or the intestine of so large a proportion of the cases as to justify the conclusion that the virus is always present upon these mucous surfaces in patients suffering from poliomyelitis during the acute stage of the disease and it is probable that the disease is conveyed from one subject to another by means of the secretion of these mucous membranes Similarly the presence of the virus has been proved in patients suffering from the abortive form of the disease without nervous symptoms and in apparently healthy contacts who thus serve as virus carriers

The researches of Hurst and Fairbrother have established that after intranasal inoculation the virus probably reaches the nervous system by way of the olfactory nerve fibers the olfactory bulb and tract It proceeds to travel along nerve fibers to the mid brain and thence by both motor and sensory axones to the spinal cord reaching the motor nuclei of the brain stem and the anterior horn cells of the spinal cord simultaneously at many levels causing widespread paralysis These workers conclude that the cerebrospinal fluid and the leptomeninges play no important part in the dissemination of the virus and that meningitis is not the primary lesion of the disease

It is probable that in man the virus usually reaches the nervous system from the nasal mucosa by the olfactory route described and Faber has made the interesting suggestion that certain symptoms hitherto regarded as general symptoms of infection are really due to invasion of the interbrain and hypothalamus by the virus and disturbance of the vegetative centers situated in this region Such symptoms include apprehensiveness and anxiety drowsiness and insomnia sweating flushing

the first year is acquired from the parent and that the rarity of the malady in adult life is due either to all the susceptibles having been picked out by the disease in childhood or to the majority of the community having been protected by the occurrence of an abortive form of the disease without nervous manifestations or possibly without symptoms of any kind in early life The sexes are equally affected and heredity is not a factor

The disease is much more prevalent during the hotter months of the summer usually the months of August and September in the northern hemisphere and the months of March and April in the southern hemisphere The incubation period is short and usually is from one to four days

Epidemicity

Though usually sporadic with great difficulty in tracing any source of infection the disease may become epidemic The first important epidemic was described by Medin at Stockholm in 1887 Another occurred in Rutland Massachusetts in 1894, and in Sweden and Norway in 1899 a very large epidemic occurred which was investigated by Wickman Since this time many other epidemics have been reported from all parts of the world These epidemics have proved that the disease spreads along the paths of human intercourse only and that it is spread by individuals who have contracted the disease or by those who are carriers of the microorganism No other factors in the spread of the malady are known There seems to be little or no tendency for the disease to occur in institutions or to spread through the inhabitants of an institution There is no evidence of any spread from school infection

The incubation period is difficult to assess Aycock and Luther conclude that it falls within a period of from six to twenty days

Experimental Pathology

In 1909 Landsteiner and Popper and several other investigators succeeded in transmitting acute poliomyelitis to monkeys by the intraperitoneal injection of an emulsion of the spinal cord from a case of that disease In the following year Flexner and Lewis by intracerebral injection of a similar emulsion were able to transmit the disease through a series of monkeys In 1913 Flexner and Noguchi claimed to have cultivated the organism of poliomyelitis under anaerobic conditions upon a mixture of ascitic fluid and fresh kidney in the form of minute globoid

both by the injection of emulsions of dried spinal cords from cases of the disease as in rabies and also by the injection of much diluted virus

Attempts are now being made in the United States to produce immunity in man by similar methods

Morbid Anatomy

The essential pathological change which occurs in the nervous system in acute poliomyelitis is an acute inflammation of the interstitial tissue



FIG 7—Section of the ventral horn from the lumbar cord from a case of rapidly fatal poliomyelitis stained with hematoxylin The acute inflammatory lesion is well shown with thrombosis of the vessel necrosis lymphocyte muffing and exudation and disappearance of the nerve cells From a photograph by Dr Greenfield

especially of the gray matter with local destruction of the nerve elements according to the severity of the inflammation and also a general toxic affection of the nerve cells (Figs 6 7 8 9 and 10) In the acute stage the pia mater of the affected region of the nervous system is infiltrated with small round cells some of which escape into the cerebrospinal fluid giving rise to the lymphocytosis of that fluid which is characteristic of poliomyelitis early in the acute stage All the vessels of the affected region are engorged and small hemorrhages are not uncommon The vessels are

tachycardia hyperesthesia vomiting and fever These are the symptoms of the first phase The second phase according to Faber is dominated by sensory symptoms especially pain owing to involvement of the posterior spinal ganglia and posterior horns of gray matter In the

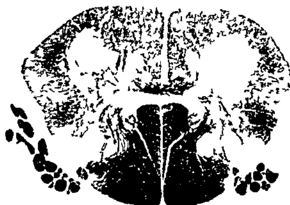


Fig 6—Section of the lumbar spinal cord from a case of poliomyelitis stained by the Weigert Pal method The pale areas in the ventral horns indicate the destruction of the gray network and of the ventral horns The degenerate ventral roots seen in cross section are well contrasted with the normal dorsal roots From a photograph by Dr Greenfield

third phase the onset of paralysis indicates that the virus has reached the anterior horn cells

While it is probable that in man the virus usually reaches the nervous system by the olfactory route other routes may be used exceptionally Thus Aycock and Luther have reported 16 cases in which poliomyelitis developed between the seventh and the eighteenth days after tonsillectomy which suggests that the raw surface of the tonsilar bed was the portal of entry

Immunity

After recovery from poliomyelitis both natural and experimental active immunity is developed and Netter and Levaditi have shown that this immunity is associated with active principles occurring in the blood which neutralize the virus Artificial immunity can be produced in monkeys

ample in the commonly occurring lesion of the ventral gray matter of the spinal cord secondary degeneration occurs in the efferent fibers of the anterior roots and peripheral nerves corresponding and also in the antero lateral tracts Subsequently the affected region becomes reduced in size and sclerosed from neuroglial proliferation

The muscles which are innervated from the affected region waste com

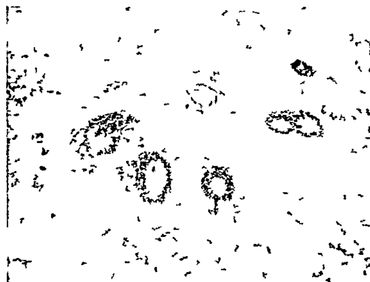


Fig 9 —Section of the ventral horn from a recent case of poliomyelitis stained with hematoxylin Blood vessels are seen in transverse section showing lymphocyte mufing and there is general lymphocytic exudation *From a photograph by Dr Greenfield*

pletely or partially according to the degree of destruction of the nerve cells (Fig 11) Some of the muscles such as the biceps humerus seem always to undergo a fibrous degeneration while others such as the gastrocnemius undergo a fatty degeneration The muscle fibers of the muscle spindles do not degenerate and contain a normal nerve fiber

Cerebrospinal Fluid — In the early days of the disease when paralysis has appeared there is invariably a lymphocytosis from a moderate increase to a very large increase of cells the albumin content is increased the chlorides are present in normal amount and the reduction of Fehling s solution is normal The fluid is clear and under abnormally high pressure The lymphocytosis is however evanescent and the cell count usually drops to normal at the end of a fortnight It is stated however that in

surrounded by numerous small round cells which produce a remarkable appearance which has been termed cuffing or muffing of the vessels A similar condition of the vessels occurs in rabies in lethargic encephalitis and in syphilis Sometimes thrombosis occurs in the vessels and this in

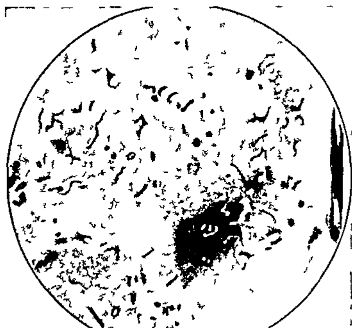


FIG 8—Section of the ventral horn from a recent case of poliomyelitis stained with hematoxylin The acute inflammation lymphocytic infiltration and perivascular muffing are well shown From a photograph by Dr Greenfield

addition to the acute inflammation and subsequent necrosis is the cause of the softening of the affected region which is often present In the gray matter in addition to the vascular changes above described many of the nerve cells are seen to be surrounded by small round cells and neurophages derived from the glia elements are seen adherent to the nerve cells and actively destroying them These changes though most marked in the gray matter are by no means there confined and may occur anywhere within the central nervous system both in gray and in white matter and they may also occur in the posterior root ganglia

When the stage of acute inflammation subsides it leaves a local necrosis which according to the severity of the initial inflammation may be so extensive as to destroy completely the affected region or so slight as to allow of almost complete recovery of function Secondary degeneration occurs according to the nerve cells which have been destroyed For ex

individual who has been in contact with a frank case or with a carrier may develop immune bodies in his blood without having had any symptoms of illness. Such a person may be described as having had a subclinical infection. (2) It is probable that in other cases symptoms of



FIG 11 —Section of a muscle which had been partly paralyzed from a case of poliomyelitis of some standing stained with hematoxylin. The atrophy of many of the fibers and the secondary fibrosis are well shown. From a photograph by Dr Greenfield

a general infection occur but are followed by recovery without the virus having reached the nervous system. Such are abortive cases. (3) There is good evidence that in a large proportion of cases — in some epidemics between 70 and 75 per cent — the infection reaches the nervous system and an excess of cells is found in the cerebrospinal fluid but recovery occurs without paralysis developing. Such patients never pass beyond the preparalytic stage and may be described as preparalytic cases. (4) Finally there are the frank paralytic cases.

Wickman recognized seven types of poliomyelitis clinically distinguishable namely (1) spinal form (2) brain stem form (3) cerebellar form

the preparalytic period the cells present are chiefly polymorphonuclear cells and that this condition rapidly changes

Blood — In the early stages of the disease there is a constant and very marked polymorphonuclear leukocytosis which may reach as high as



FIG 10 —Section of the ventral horn from a case of recent poliomyelitis stained with hematoxylin Blood vessels with lymphocyte cuffing are seen in longitudinal section From a photograph by Dr Greenfield

30 000 and there is lymphocytic leukopenia This leukocytosis soon disappears when the fever abates

Lymphoid Tissues — All cases of poliomyelitis that have been examined by necropsy show striking hyperplasia of the lymphoid tissues including the tonsils the thymus the lymphoid tissue of the intestine and the superficial and deep lymphatic glands The spleen is enlarged and the malpighian bodies prominent In the liver hyalin focal necrosis of liver cells with regeneration and invasion by lymphocytes and polymorphonuclear cells occurs

Clinical Aspect

Recent additions to our knowledge have led to the recognition of four different reactions to infection with the virus of poliomyelitis (1) An

spread to other regions This sudden extension of paralysis after the lapse of days has been observed in experimental poliomyelitis in monkeys

The paralysis is generally much more widely spread at the onset than it is destined to be permanently Thus all four limbs may be at first completely helpless and there may be later complete recovery in all but one limb Here the widely spread temporary paralysis must be due to a toxic and recoverable affection of the nerve cells whereas the permanent palsy is the result of an actual destruction of the cells by a necrotic lesion The paralysis may affect any of the muscles of the body but those of the legs are by far the most commonly involved The trunk muscles may be affected alone giving rise to marked spinal deformity usually of a scoliotic or kyphoscoliotic type It is probable that many cases of lateral curvature of the spine have their origin in poliomyelitis confined to the dorsal region of the cord

The narrowing down of the initial widely spread paralysis begins to show itself after the end of the first week and any muscle which is going to recover useful power will have done so before the end of the third month It will occasionally be noticed that the deep reflexes are not lost in the paralyzed region in the early days of the disease and where this retention of the deep reflexes obtains recovery is always complete The paralyzed muscles undergo atrophy which is more rapid and complete in those which are to show no subsequent recovery To electrical tests they show a reaction of degeneration They are flaccid from the first and in the course of time tend to develop a degree of fibrotic contracture Any muscles which show response to faradism three weeks after the onset will completely recover There is usually a considerable degree of vasomotor palsy when a limb is paralyzed and there may be some retardation of growth

Considerable deformities of the body and limbs may arise as the result of the loss of support which results from the paralysis from the action of unopposed muscles and from the occurrence of contractures Such deformities may involve actual dislocation of joints as in the shoulder joint where the deltoid is paralyzed and the pectorals escape

In rare cases the local lesion of the spinal cord is not confined to the gray matter but involves also the contiguous white matter of the lateral column giving rise to signs of lesion of the pyramidal tract and perhaps also of other neighboring tracts For example cases have occurred in which a typical poliomyelitis of one upper extremity has been associated with a synchronous spastic paralysis of the lower extremity of the same side with increased reflexes and an extensor response in the plantar reflex Obviously such an extension of the lesion to the white matter neighboring upon the ventral horn may give rise to loss of pain and temperature sensibility be

(4) cerebral form (5) meningitic form (6) neuritic form (7) abortive form It is now regarded as extremely doubtful whether acute inflammatory lesions of either the cerebral hemispheres or the cerebellum are due to the virus of poliomyelitis nor is there convincing evidence that a purely neuritic form occurs The meningitic form includes both preparalytic cases and cases in which symptoms of meningeal irritation of a pronounced character precede or coincide with paralysis The 'spinal and brain stem forms comprise all the manifestations of the incidence of the infection upon the neuraxis

The onset is abrupt and usually is accompanied by fever which develops rapidly and lasts but a few days the whole febrile movement rarely lasting longer than seven days The fever may be ushered in by a chill in adults and by convulsions in children and especially in infants General malaise headache and pains in the limbs are complained of by patients who are old enough to describe their symptoms Gastrointestinal disturbances such as anorexia vomiting and diarrhea are common When the onset is severe there may be delirium and stupor with head retraction pain and rigidity on passive movement of the neck and back Kernig s sign and incontinence Usually the skin is flushed and the expression bright the latter point contrasting with the expression of many forms of meningitis The muscles are often tender to pressure and the joints painful on movement and these signs with the spontaneous pains may persist for many weeks In a minority of the cases the general symptoms are absent or so slight as to escape notice and the nervous symptoms are the first evidence of illness This absence of general symptoms and of fever seems to occur only in the spinal form of the disease and in children

Spinal Type

In young children the paralysis is often not apparent until the second or third day after the onset In older children and in adults the paralysis usually is present within twenty four hours of the onset The paralysis is always of the complete flaccid variety with loss of the deep reflexes in the region of the paralysis and subsequent atrophy of the muscles The paralysis develops very rapidly in most of the cases and seems to have its full limit of distribution at the moment of its appearance In some cases however commencing in the legs the paralysis spreads slowly upwards and gradually affects trunk and arms successively (ascending or Landry type) or conversely it may commence in the arms and spread to trunk and legs afterwards (descending type) In rare cases the paralysis after remaining stationary for from two days to a fortnight may suddenly

prognostic indication that the muscles concerned with the reflex will entirely recover. When poor recovery occurs in a muscle it is the rule for the deep reflex to remain permanently absent even though some voluntary power is regained.

It has already been pointed out that an extensor response may be seen in the plantar reflex in cases where an extension of the inflammatory process has involved the crossed pyramidal tract. On the other hand an extensor response obviously will always obtain where the flexors of the toes are permanently paralyzed and the extensors of the toes escape since the extensors are then the only muscles which can respond.

Course.—The febrile stage with general symptoms may be so little marked as to escape notice and this is most often seen in young children but rarely if ever in adults or it may be exceedingly severe with convulsions or delirium and stupor. Usually the temperature abates upon the third day and the entire febrile movement does not last more than a week. The paralysis most often appears on the second or third day in children and in adults upon the second day. When first apparent the paralysis usually is complete and does not subsequently spread. In rare cases it is slight when first noticed and it rapidly deepens to its full extent. Still less frequently it begins locally and spreads constituting an ascending or descending type and this has been met with most often in epidemics such as occurred in Scandinavia in 1905.

Sensory disturbances and sphincter trouble often are absent and when present they usually pass off within a few days of the onset of the paralysis but in some cases much pain tenderness of the muscles and pain on moving the joints may persist for many weeks. In very rare cases a further attack of paralysis occurs within a fortnight of the onset of the original paralysis and this obviously is due to a recrudescence of the infection.

Most commonly within a few days of the onset of the paralysis a very considerable remission occurs and the paralysis becomes much narrowed down in its limits thus with an initial paralysis of all four limbs and trunk the limbs recovered rapidly leaving a permanent partial paralysis of the trunk and in a case where both legs were paralyzed the one recovered power within the first week leaving the other permanently crippled. Sometimes however there is no rapid improvement or narrowing of the region of paralysis whatever. These results are to be explained pathologically in that those regions where the paralysis is due to a toxic effect upon the nerve cells which is a recoverable lesion rapidly recover whereas recovery does not take place where the nerve cells have been destroyed by necrosis following the inflammatory lesion.

The paralysis remaining after the rapid improvement is final and ad

low the level of the lesion upon the whole of the opposite side (Brown Sequard s syndrome)

In still rarer cases there may be extensive involvement of the white matter of the whole transverse area of the spinal cord giving rise to signs of a total transverse lesion namely complete flaccid palsy with extensor responses and loss of sensibility below the level of the lesion and total sphincter paralysis Such cases have been recorded by Batten Sachs, Netter and Levaditi and by Strumpell and I have seen two such cases Paralysis of the cervical sympathetic is not infrequently met with in those cases where the lower cervical and first dorsal segments are involved with the usual signs of a small pupil and narrow palpebral aperture on the affected side It is generally a transient phenomenon

When the limbs are affected paralysis of the blood vessels most marked at the periphery is the rule and there is permanent coldness to touch and pinkness or blueness of the skin which is greatly increased by exposure to cold This condition may cause considerable suffering unless the limb is most carefully clad

In the course of time the bones of the affected limb may show conspicuous smallness from retardation of growth if the disease has been incident during the period of growth The bones become unduly fragile from a rarefying process and their ridges and bony prominences atrophy and do not further develop but there is never the same degree of arrest of growth of a limb as is sometimes seen in infantile hemiplegia Atrophy of the skin and nails scarring and loss of the subcutaneous tissue are frequently seen and are presumably the result of the vasomotor paralysis and of disuse and of chilblains

Disturbances of sensibility of an objective kind are rare and are almost always transient and amount to a blunting of pain and temperature sensibility doubtless from involvement of the spinothalamic tracts which are contiguous to the ventral horns Subjective disturbances are common and may consist in severe local pains in the limbs back or neck Tenderness of the muscles and pain on moving the joints sometimes are very prominent and may persist for many weeks Sphincter paralysis is quite common in the early stages where the lumbosacral enlargement is affected but it is always transient and lasts but a short time

The reflexes both superficial and deep are at first lost in the affected region and indeed are generally absent throughout the body in the early stages of a severe case from the general toxic effect upon the nervous system In the later stages they return or remain permanently absent according as the muscles recover or not Any sign of a returning reflex either deep or superficial in the early days of the illness is a most useful

limb introduces a disability which cannot be compensated for by other muscles and cannot be dodged by acquired aptitude on the part of the patient neither can it be assisted by any mechanical contrivance

Second attacks of poliomyelitis are exceedingly rare but two such cases have been recorded by Eshner and by Sanz The occurrence of progressive muscular atrophy in subjects who have in early life been afflicted with poliomyelitis is not very rare and it is usual for the progressive atrophy to commence in the region originally affected by the poliomyelitis Potts has recorded a series of twenty-eight such cases and several others are to be found among the records of the National Hospital

Diagnosis — During the stage of general pyrexial symptoms and before the nervous manifestations appear a definite diagnosis can hardly be made but it may be suggested by the time of year by the prevalence of an epidemic and by the combination of a polymorphonuclear leukocytosis in the blood with a lymphocytosis in the cerebrospinal fluid Gay and Lucas have examined the cerebrospinal fluid in eleven human cases in the preparalytic stage and found a leukocytosis ranging from 55 to 580 per cubic millimeter in all with a percentage of mononuclear cells of from 75 to 100 the remainder being polymorphonuclear cells

When the paralysis first sets in the diagnosis has to be made from acute rheumatism in which the painful joints may cause an appearance of severe paralysis An examination of the reflexes will at once distinguish the two conditions for both the superficial and the deep reflexes are brisk in rheumatism and lost in poliomyelitis In the same way syphilitic pseudoparalysis (acute syphilitic epiphysitis) may be diagnosed from poliomyelitis From acute polyneuritis and Landry s paralysis both of which maladies may have a pyrexial onset with similar general symptoms poliomyelitis generally can be distinguished by the sudden onset of the paralysis and by the absence of any spreading tendency and probably by the lymphocytosis in the cerebrospinal fluid and later on in the case by the permanent atrophic paralysis In the rare spreading types of poliomyelitis the latter two points alone serve to make the diagnosis

From almost all of the local lesions of the spinal cord membranes and roots whether these are of rapid onset as for example hematomyelia and acute myelitis or of slow onset such as tumor inflammation and pressure poliomyelitis is at once distinguished by the absence of the conspicuous sensory loss and sphincter trouble which accompany the former diseases Acute anterior radicular neuritis is very difficult to distinguish from poliomyelitis but the age of the patient the limitation of the paralysis to the distribution of one or two roots and the absence of spinal lymphocytosis are important indications

mits of such improvement only as may occur from the recovery of a few cells which have escaped destruction upon the confines of the inflammatory lesions and such recovery is very slow and never reaches more than a slight degree A certain slow improvement in those paralyzed muscles which retain some voluntary power is often observable and is referable to hyper trophy of function in those elements which remain and to the acquisition of the aptitude which necessity brings about On the other hand children afflicted with this disease during the period of active growth often will show what seems to be a progressive diminution of power in the weak muscles which is in reality a relative failure of these muscles under the strain of the increasing weight and length of the body and limbs

Death is uncommon at any stage in the spinal form of poliomyelitis except during epidemics when severe general symptoms are followed by widely spread paralysis involving all the respiratory muscles and in these cases it takes place on the first day of appearance of the paralysis Weak ness of the respiratory muscles and especially total intercostal palsy are not infrequently indirect causes of death even at long periods after the onset if bronchitis or bronchopneumonia occurs

Prognosis — It is doubtful whether complete recovery occurs in any case of poliomyelitis in which paralysis has once set in Though in some cases recovery may be nearly complete yet there seems always to be some region in which permanent muscular atrophy persists and in cases which otherwise clear up this is frequently in the spinal muscles giving rise to a lateral curvature From this condition of nearly complete recovery to one in which there is not the slightest recovery from the initial paralysis there is every gradation

The prognosis is not influenced by the severity or otherwise of the general symptoms for the paralysis may be slight where the general symp toms are severe and vice versa Incomplete paralysis or the presence of reflex action either superficial or deep in any region at the end of the first week after the paralysis has set in is a sure indication that useful recovery will occur in that region Those regions which remain completely paralyzed for several weeks after the onset are certain to remain permanently dis abled

The prognosis as to the eventual usefulness of disabled limbs or as to eventual power of walking depends upon a consideration of the muscles which are permanently paralyzed as to whether they are essential muscles or not and whether they can be assisted or supplanted by any mechanical apparatus which is light enough for the weak limbs to carry For example the gluteal muscles are absolutely essential for the projection of the leg in walking and their permanent involvement in poliomyelitis of the lower

limb introduces a disability which cannot be compensated for by other muscles and cannot be dodged by acquired aptitude on the part of the patient neither can it be assisted by any mechanical contrivance

Second attacks of poliomyelitis are exceedingly rare but two such cases have been recorded by Eshner and by Sanz The occurrence of progressive muscular atrophy in subjects who have in early life been afflicted with poliomyelitis is not very rare and it is usual for the progressive atrophy to commence in the region originally affected by the poliomyelitis Potts has recorded a series of twenty-eight such cases and several others are to be found among the records of the National Hospital

Diagnosis — During the stage of general pyrexial symptoms and before the nervous manifestations appear a definite diagnosis can hardly be made but it may be suggested by the time of year by the prevalence of an epidemic and by the combination of a polymorphonuclear leukocytosis in the blood with a lymphocytosis in the cerebrospinal fluid Gay and Lucas have examined the cerebrospinal fluid in eleven human cases in the preparalytic stage and found a leukocytosis ranging from 55 to 580 per cubic millimeter in all with a percentage of mononuclear cells of from 75 to 100 the remainder being polymorphonuclear cells

When the paralysis first sets in the diagnosis has to be made from acute rheumatism in which the painful joints may cause an appearance of severe paralysis An examination of the reflexes will at once distinguish the two conditions for both the superficial and the deep reflexes are brisk in rheumatism and lost in poliomyelitis In the same way syphilitic pseudoparalysis (acute syphilitic epiphysitis) may be diagnosed from poliomyelitis From acute polyneuritis and Landry s paralysis both of which maladies may have a pyrexial onset with similar general symptoms poliomyelitis generally can be distinguished by the sudden onset of the paralysis and by the absence of any spreading tendency and probably by the lymphocytosis in the cerebrospinal fluid and later on in the case by the permanent atrophic paralysis In the rare spreading types of poliomyelitis the latter two points alone serve to make the diagnosis

From almost all of the local lesions of the spinal cord membranes and roots whether these are of rapid onset as for example hematomyelia and acute myelitis or of slow onset such as tumor inflammation and pressure poliomyelitis is at once distinguished by *the absence of the conspicuous sensory loss and sphincter trouble* which accompany the former diseases Acute anterior radicular neuritis is very difficult to distinguish from poliomyelitis but the age of the patient the limitation of the paralysis to the distribution of one or two roots and the absence of spinal lymphocytosis are important indications

In the final stage of permanent muscular paralysis and atrophy deformities and contractures poliomyelitis presents little difficulty of diagnosis but it should be borne in mind how frequently deformities of the trunk and especially lateral curvature of the spine have their origin in slight attacks of this malady where the lesions are confined to the dorsal region

Treatment — In the acute stage the patient should be kept at rest upon a soft bed and fed upon a diet suitable to the febrile condition Since the malady is an infectious specific fever and since the virus is known to exist upon the nasal, buccal and respiratory mucous membranes and is presumably spread therefrom bed and utensil isolation is necessary with sterilization of any contamination from the mucous membranes and mild daily disinfection of the mouth and nose

Lumbar puncture should be performed at once and repeated daily for four days and the fluid freely drawn This operation by itself often relieves the most acute symptoms and is to be used not only as a method of diagnosis but also as a means of treatment Salicylates especially in the form of aspirin will relieve the pain and fever and seem to be decidedly beneficial If pain be very severe there is no contra indication to the use of morphia

If the respiratory muscles are seriously involved belladonna or atropin are of great service both in stimulating the respiratory mechanism and in checking accumulation of bronchial secretions

The Drinker respirator enables artificial respiration to be maintained continuously for days It has been used successfully in cases in which the respiratory muscles have been temporarily paralyzed but have subsequently recovered and which would have been fatal in the absence of such mechanical aid but when the respiratory muscles do not recover, the doctor is faced by a difficult decision since the patient cannot survive outside the respirator

Serum Treatment — Flexner and Amoss have shown that intrathecal injections of an immune serum are effective when introduced in the pre paralytic stage in delaying and preventing poliomyelitic infection in the monkey An immune serum can be obtained from the blood of any patient who has passed through an attack of poliomyelitis The length of time after the attack is not important, for it has been shown that the blood preserves its antitoxic properties for several years after the attack From such a patient 30 c c or more of blood are obtained by venepuncture The serum is separated by allowing the blood to clot and 10 to 30 c c of this serum are injected by lumbar puncture daily after withdrawing some of the cerebrospinal fluid The serum may also be given intravenously at the same time

This treatment with serum from patients who had the disease has been tried on a large scale in human cases in the United States and elsewhere *Park has published a comparison between 519 treated and 408 untreated* cases in the same epidemic There was no reduction in the mortality rate nor in the incidence of paralysis in the treated cases

Rest and Posture — It is all important to secure as complete physio logical rest as is possible for the weak or paralyzed muscles for some time after the onset Even in the slightest cases the patient should be kept in bed for at least three weeks during which time attempts at volitional move ments should be discouraged The posture of the paralyzed region should be such as to secure the relaxation of the paralyzed muscles for if the paralyzed muscles are kept stretched by the action of opponent muscles which are paralyzed recovery is greatly hindered Appropriate postures can be secured by pillows sandbags splints and other devices

After a few weeks have elapsed massage and passive movements should be regularly employed and reeducationary exercises commenced where there is sufficient power Electrical treatment in any form is of very doubtful value and since strong currents are often requisite to ob tain any contraction of the affected muscles its application in children often causes such fright and distress as to do actual harm

Reeducation should be assisted by every appropriate mechanical de vice but it must be carefully borne in mind that every mechanical ap paratus which overweights the weak limb places a millstone around the neck of recovery The lightest possible shoes should be worn and if splints are indicated the excellent and almost weightless moulded cellu loid splints should be employed to the absolute exclusion of all heavier varieties In the reeducation of the legs for walking a walking machine on wheels is a necessity Contractures and deformities which hinder useful action should be dealt with by passive movements splinting tenot omies and other surgical procedures

Prophylaxis — Passive immunization by means of 10–20 c c of con valescent serum may confer immunity lasting for 2 or 3 weeks and this method may be used to protect children in an epidemic If convalescent serum is unobtainable the pooled blood serum of several normal adults may be effective since the blood serum of many adults possesses the power of neutralizing the virus *Immune horse serum may be similarly used Attempts are being made to produce immunity by means of a* vaccine There is experimental evidence that spraying the nose and throat with ½ per cent picric acid and other chemicals protects against the infection This may be carried out every other day for a week and thereafter weekly

The Brain Stem Form

In this type the incidence of the lesions is upon the gray matter of the brain stem from the medulla to the region of the red nucleus The general symptoms of the onset are as in the spinal form but there is likely to be in addition head retraction and stiffness of the neck muscles In place of the paralysis of trunk and limbs there is bulbar paralysis facial paralysis trigeminal paralysis or ocular paralysis according to the situation of the lesions There may be nystagmus if any of the cerebellar connections are involved and tremors if the red nuclei are affected An extensive lesion of the medulla itself proves very rapidly fatal in poliomyelitis Lesions of the upper brain stem are more commonly survived and the resulting clinical pictures are in order of frequency of occurrence facial paralysis spastic tremulousness from involvement of the upper part of the brain stem and lastly ocular paralysis with nystagmus Any combination of these forms may occur with one another and with the spinal form of the disease

It is likely that many of the cases of acquired strabismus following convulsion or febrile illness in children are of this nature Special mention is necessary of the facial paralysis which occurs in poliomyelitis and which usually is attributed to a lesion of the facial nucleus When occurring in conjunction with the spinal form of the disease its cause is obvious but when it arises as an isolated event its origin in poliomyelitis is difficult to determine Batten has pointed out that the incidence of facial paralysis in children corresponds to the seasonal incidence of poliomyelitis

The Meningitic Type

One of the most interesting types of poliomyelitis which frequently gives considerable difficulty in diagnosis is the meningitic form of the disease The onset is sudden and is attended occasionally by convulsion and coma The temperature is raised and may remain high for days and the usual symptoms of meningitis are present Headache and vomiting occur The neck is stiff and the head may be retracted there may be opisthotonos and rigidity of the legs and Kernig s signs are commonly present Lumbar puncture reveals a cerebrospinal fluid clear and under pressure which on cytological examination may at first show no abnormality but as the days elapse will show an increasing number of lymphocytes an increased amount of albumin and a diminished sugar reaction The chloride content of the fluid is normal a point of distinction from tuberculous meningitis in which it is markedly diminished

There are certain clinical points which will sometimes serve to distin

guish this type of the disease from other conditions of lymphocytic meningitis In many cases careful examination has revealed a local flaccid palsy of some part of a limb and if such a palsy is present it should go very far to settle the diagnosis Again a flushed face and bright expression are characteristic of poliomyelitis and contrast strongly with the pale, dull facies of tuberculous meningitis Lastly it is the rule for the meningitic form of poliomyelitis to recover and leave no intracranial sequelæ and this will distinguish it from the invariably fatal tuberculous meningitis

The other common forms of lymphocytic meningitis are those due to tubercle sinus thrombosis mumps measles lethargic encephalitis and syphilis In any questionable case the discovery of the tubercle bacillus in the spinal fluid will settle the diagnosis and a mixed polymorphonuclear and lymphocyte count with high lymphocytes is characteristic of tuberculosis The history in the case of mumps and measles and the Wassermann reaction in the case of syphilis are important guides in the diagnosis The treatment is that of poliomyelitis and meningitis in general

The Abortive Form

This type of poliomyelitis may be described as corresponding with the initial stage of febrile and general symptoms before the appearance of the paralysis The general bodily infection with the virus occurs but it does not reach the nervous system or affects it so little as to cause no characteristic symptoms The attack as a rule is acute with fever headache and malaise and in some cases slight nervous symptoms such as rigidity of the neck pain in the neck and back and limbs Paræsthesiæ occur These symptoms are not followed by paralysis and recovery occurs within a few days Except when poliomyelitis becomes epidemic it is hardly possible to detect the abortive forms of the disease Nevertheless since an epidemic of this disease among a population seems to immunize the whole population and remove all susceptibles so that in a subsequent epidemic only those born since the previous epidemic are affected it seems clear that affection by the slight abortive form of the disease was the cause of the immunity

Doubtless in a country such as England where poliomyelitis never has been epidemic the abortive form occurs frequently enough among the commonly occurring short febrile illnesses of children which at present do not admit of definite diagnosis

CHAPTER XX

INTRINSIC DISEASES OF THE SPINAL CORD

(Continued)

By J. Godwin Greenfield

Table of Contents

VII

Syringomyelia Syringobulbia and Hydromyelia

By J GODWIN GREENFIELD

Definition —The name, syringomyelia, meaning a tubular condition of the spinal cord is given to a slowly progressive disease which usually makes its appearance late in the second or in the third decade of life

In its typical form the disease is characterized clinically by atrophic paralysis of muscles or muscle groups in the upper limbs and segmental bands of analgesia and thermanesthesia usually without tactile anesthesia on the limbs trunk and head Some degree of spastic paraplegia is also present in many cases Trophic changes in the skin and Charcot joints may be associated symptoms When syringobulbia is also present nystagmus and various paralyses of the lower cranial nerves are found The anatomical basis of the disease is the presence of a tubular cavity in the spinal cord which most often runs in the gray commissure and extends into the lateral or dorsal horns In syringobulbia one or more slit like cavities are present in the medulla

During the present century syringomyelia as an idiopathic disease has been distinguished from hydromyelia on the one hand and from local cavitation of the cord due to central necrosis of vascular inflammatory or neoplastic origin on the other In many cases however this distinction is by no means easy and in some it may be impossible since hydromyelia may by extension of the cavity go on to syringomyelia and tumors of the cord may be associated with typical syringomyelic cavities above or below them

Pathological Anatomy

Syringomyelia—When exposed by laminectomy a syringomyelic cord appears larger than normal and fluctuates on palpation During life the cavity is usually tense and when punctured fluid may escape from it under pressure On postmortem examination it readily collapses and in extreme cases the cord then appears over a considerable length as a flattened ribbon The condition commonly extends upward for a varying distance into the medulla (syringobulbia) and much more rarely into the pons and midbrain On cross section of the cord the cavity usually is found to be more extensive than can be gauged by an external examination Very commonly it begins in the upper cervical segments of the cord and extends down to the lower thoracic or the upper lumbar segments sparing some or all of the lumbar segments The cavitation affects chiefly or entirely the gray matter of the cord especially the gray commissure and the posterior horns but extensions into one or both lateral horns are common In many cases it runs backward into the dorsal columns often with its greatest extent in the line of the dorso median septum An anterior extension in the midline is also fairly common

When lateral posterior, and anterior extensions are combined the cross section of the cavity has a cruciform appearance. Extensions along the dorsal horns may run to the surface of the cord, and the cavity is then arciform (Fig 1b). Or it may reach the pia mater along the line of the dorso median septum or in the ventro median fissure. The anterior cornua are commonly invaded by the cavity, especially in the cervical cord. *Not infrequently the cavity appears double on cross section over* some part of its extent, but it is usually found in such cases that both cavities communicate with a single cavity at a higher or lower level.

Microscopical examination shows the connection of the cavity with the central canal of the spinal cord to be very variable. Even in a single case the cavity may run separate from the central canal in some segments and blend with it in others. The smaller cavities usually lie behind the central canal and may make no connection with it. But the larger and more extensive cavities usually blend with the central canal over several segments, where short rows of ependymal cells can be seen lining the anterior wall. Above and more often below, the cavity there is usually some distension of the central canal for a few segments. This is the usual appearance in the lumbar segments of a syringomyelic cord. On the other hand, the first cervical segment very often contains neither cavity nor central canal but rather an irregular clump of ependymal cells. At lower levels in the cervical cord the cavity passes laterally into the gray matter, often destroying the postero lateral group of cells in the lower cervical segments. This supplies the more peripheral muscles of the upper limbs. The intermedio-lateral tract in the two or three uppermost thoracic segments also is often destroyed with resulting paralysis of the sympathetic efferents to the head, neck, and upper limbs. The ventro mesial group of cells in the anterior cornua is less often directly involved in the cavitation.

In severe cases the cord may consist, especially in the lower cervical and upper thoracic segments of a narrow zone of nervous tissue surrounding the cavity. In this zone the anterior horns may be the only recognizable gray matter.

The wall of the cavity varies greatly in character in different cases and even in different segments of the same case. It is formed of neuroglial cells and fibers but in some cases a thin collagenous layer lines the inner surface of this or scattered collagenous fibers are seen in the neuroglial tissue. This neuroglial wall usually varies from 200 to 500μ in thickness but may exceed this. It may be concentric, and of even

thickness over several segments or may show irregular pads or zones of thickening and areas such as those under rows of ependymal cells where it is much thinner In some cases it may be ragged suggesting recent tearing of neuroglial tissue an appearance which often is due no doubt to postmortem artefact but in some cases appears to be pre existing The neuroglial fibers which compose the wall are largely orientated in the longitudinal axis of the cord (Puusepp 1933) In some areas the wall consists chiefly of fusiform (piloid) astrocytes with polar processes The zone around the wall may be edematous and contain swollen bodied astrocytes and edema may be responsible for secondary irregular cavitation external to the main cavity The meninges may be slightly thickened but often appear normal The intra medullary blood vessels where they lie in or near the cavity often show hyaline thickening of their walls and it is not unusual to see such a vessel passing for a short distance into the lumen of the cavity

It is the author s experience that syringomyelia is rarely found in an uncomplicated form on postmortem examination Either it is associated with tumor of the cord or with syphilitic meningomyelitis or it is combined with an abnormality at the medullary level which may be either syringobulbia or the Arnold Chiari malformation Syringomyelia or syringobulbia or both are occasionally found in patients dying from tumors of the cerebral hemispheres The reason for this may well be that uncomplicated syringomyelia is usually a very slowly progressive disease which of itself does little to shorten life

Syringobulbia —Syringobulbia is usually associated with rather extensive cavitation of the cord It must be distinguished from cavitation of the medulla as a result of ischemic necrosis e g after thrombosis of the posterior inferior cerebellar artery or cavitation in or beside a tumor The cavity in the medulla is usually little more than a slit which in almost every case examined has been in one of three positions two or more slits often being present together

(1) Of these the commonest is for the slit to begin in or under the floor of the 4th ventricle between the hypoglossal and the dorsal vagal nuclei and to run in an antero lateral direction toward the descending trigeminal root and nucleus (Fig 1a) This cavity or slit may be unilateral or bilateral and may or may not communicate with the 4th ventricle Its caudal limit is usually at the level of the decussation of the pyramids where it runs out antero laterally from the tissue round the central canal with which it rarely communicates interrupting some of





Figs 1 *a* & *b* Sections across the upper medulla and cervical cord from a woman of 47 years who had symptoms of syringomyelia for twenty five years Complete analgesia in the left hand had been noticed at the age of 17 When last examined there were nystagmus on lateral deviation of the eyes analgesia of the left face and almost the whole of both sides of the neck trunk and limbs but sparing the right foot and the left leg from the knee down There was also anesthesia to light touch over the left half of the neck trunk and limbs The left hand was swollen and purplish red in color There was dorsal scoliosis

Fig 1 *a* shows the position of the cavity in the left side of the medulla and the pallor of the opposite medial fillet In Fig 1 *b* the cavity in the cervical cord is seen to extend through the gray matter of the dorsal horns almost to the pia mater

the crossing fibers of the pyramidal tract It may extend up to or above the middle of the medulla but rarely reaches its upper limit A slit of this kind will cut across the line of the descussating fibers passing from the nuclei gracilis and cuneatus to form the medial fillet It will also interrupt fibers passing from the descending nuclei of the trigeminal and vestibular nerves toward the midline and those passing dorsally from the nucleus ambiguus before they turn ventro laterally Severance of these fibers produces a characteristic symptomatology which will be discussed later The cavity often also destroys the fasciculus solitarius Secondary atro phy of the parent nerve cells results from the severance of emerging or decussating fibers it is usually clearly seen in the nuclei gracilis and cuneatus It is also not uncommon to see some degree of retrograde degeneration of an affected pyramidal tract at the level of the upper medulla that is above the level at which it is interrupted This is prob ably a very slow process and is only seen in cases with long standing hemiplegia or quadriplegia (Fig 6)



Fig 6 Section across the medulla of a man of 31 who had symptoms since the age of 26 years These were nystagmus on lateral deviation of the eyes diplopia to the right partial analgesia and thermanesthesia of the right face and left half of the body and limbs and weak ness along with diminution of the sense of vibration position and passive movements in the right arm and leg Sensibility to light touch was everywhere intact
The cavity extends out from the central canal to the region of the right pyramidal and spinothalamic tracts interrupting the decussation of the fillet There was also syringomyelia of minor degree in the cervical cord

(2) A rarer position is between the pyramidal tract and the inferior olive Such a cavity may interrupt the course of the hypoglossal nerve and, if it extends upwards to the lower pons, also that of the abducens and facial nerves on the side of the cavity (Fig 2) This cavity is rarely bilateral When extensive it may cause degeneration of the ventral part of the inferior olive as well as the dorso-external part of the pyramidal tract It may pass down dorsal to the pyramidal tract as far as its decussation



Fig 2 Section of the medulla from a case of syringomyelia with syringobulbia in a man of 47 who had symptoms since the age of 18 On examination he had paralysis of the right sixth cranial nerve complete right facial palsy and wasting of the right half of the tongue There was analgesia and thermanesthesia over the neck upper limbs and upper part of the trunk on both sides and anesthesia to light touch over the right half of this area

The section is above the lateral cavity to which the atrophy of the left medial fillet is due There is a ventral cavity between the right pyramid and inferior olive which has destroyed the right abducens and hypoglossal nerves

(3) Not infrequently a slit, usually lined by ependyma passes forward from the floor of the ventricle along the median raphe for a variable distance This slit which may be little more than an exaggeration of the normal median groove on the floor of the ventricle, only interrupts the fibers from the descending vestibular root which cross the midline

to the contra lateral medial longitudinal fasciculus It is very commonly seen along with a slit in the position first described

Cavities in the pons may be limited to that level of the brain stem or may pass upward to the midbrain or downward to the medulla They usually lie in the tegmentum but Spiller described a cavity in the line of the pyramidal fibers and substantia nigra with an extension upward into the internal capsule The slits or cavities in the brain stem are rarely surrounded by such firm walls as those in the spinal cord In some cases there is above the cavity a plane of neuroglial scarring through which no nerve fibers pass Such a scar may result from secondary junction of the walls of a cavity or it may be developmental in origin A similar appearance is sometimes seen in the spinal cord

As the result of interruption of tracts or destructive pressure on them various secondary degenerations are seen in the spinal cord and brain stem Degeneration of the pyramidal tracts may result from distension of a cavity in the cervical cord or from interruption at the level of the decussation in the medulla in the latter case it may be unilateral Degenerations of the dorsal columns and of the direct cerebellar tract are commonly seen in the cervical segments and some pallor of the spino thalamic tracts is usual In cases of syringobulbia with slits in the first position described the medial lemniscus on one side is usually absent in whole or in part, and there may be some disparity between the two lateral divisions of the medial longitudinal fasciculus

Hydromyelia—The name hydromyelia or hydromyelus is given to dilatations of the central canal of the cord of congenital origin They are not infrequently found in routine postmortem examinations and they occur in a large proportion of infants with spina bifida and meningo myelocele and in older patients with the Arnold Chiari malformation They are of very varied size and extent When minimal they may be only a slight dilatation of the central canal limited to a few segments most often at the cervical level or there may be a wide tubular cavity running for most of the length of the spinal cord All grades between these extremes are found The cavity may consist of an antero posterior slit when the dorso median arm of the embryonic cavity fails to close or less often of a transverse slit or it may be cruciform in cross section when all four arms remain patient In infants the commonest form seems to be triangular with a dorsal extension coming to a point in the mid line and a flattened or rugose anterior wall running more or less transversely (Fig 3) In most cases the antero posterior diameter is greater

than the transverse diameter but in the larger cavities the reverse is true The wall is lined over a large part of its surface by ependyma, but defects in this are seen, most often in the angles or in the bays of the rugose surfaces and ependymal nuclei may be seen lying deep to the surface in such situations The amount of neuroglial fibrosis in the wall varies greatly and appears to be independent of the size of the canal The defects in the ependyma are usually sealed by neuroglial thickening which may form tufts projecting into the cavity similar to those

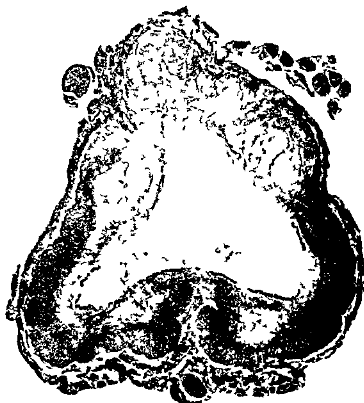


Fig 3 Hydromelus in an infant of 6 weeks with meningomyelocele and Arnold Chiari malformation The illustration shows extensive loss of ependyma with early compensatory gliosis

of granular ependymitis This appears to be a progressive process as it is rarely seen in newly born infants As such cavities cause little or no destruction of tracts or fibers they are usually asymptomatic

In juvenile and adult cases the cavities are usually more rounded and are lined partly by ependyma and partly by a concentric zone of

fibrous astrocytes (Fig 4) They thus form a link between the classical syringomyelic cavity and hydromyelia When asymptomatic they may be assigned to the latter category but when there is destruction of nerve cells and fibers associated with the characteristic symptoms of syringomyelia they may be difficult to classify In such cases the cavity is usually fairly large and has burst its ependymal lining in many places or only a few short lines of ependymal cells may remain most often in the ventral wall In some cases of the Arnold Chiari malformation the cavities resemble those of classical syringomyelia in every respect except



Fig 4 Hydromyelus in a lad of 15 year who died f respiratory paralysis due to an Arnold Chiari malformati n Ependyma is seen only on the ventral wall, and elsewhere there is a concentric zone of gliosi

that they involve the central canal for a greater part of their extent but this criterion has not the importance assigned to it by the older writers In such cases syringomyelia which is typical both clinically and pathologically appears to arise from progressive distension of a hydromyelic cavity This theory of pathogenesis is probably only true for a minority of cases of syringomyelia but it is important in relation to cases of different origin as showing the effect of tension within the cavity in enlarging it and affecting the structure of its walls The progressive neuroglial thickening round hydromyelic cavities lends no support to the old German view that in syringomyelia the neuroglial thickening is primary and the cavitation secondary to it It seems more probable that the neuro-

glial wall forms as a result of tension and other strains inside the cavity and is in fact a reparative process. That it may fail in this and sometimes be torn through in places does not invalidate this theory.

Secondary Syringomyelia.—It is usual to distinguish between the uncomplicated cases of syringomyelia, with or without syringobulbia, which are classed as primary or idiopathic, and cases in which syringomyelia is associated with other diseases of the spinal cord, which are classed as secondary syringomyelia.' Cavitation, as an end result of edema or necrosis of tissues, or in the site of an old hematomyelia, may occur in vascular, traumatic or inflammatory diseases of the spinal cord or near a spinal tumor, whether intra- or extra-medullary. Syphilis, in its meningovascular form, is especially prone to cause small cavities of this kind, and in times when tertiary syphilis was more common than it is at present there was a tendency to attribute many cases of syringomyelia to this etiology, a tendency to which the clinical similarity of the two diseases no doubt contributed. Actually syphilis appears to be a rare cause of more extensive cavitation, but we meet with occasional cases which closely resemble primary syringomyelia both clinically and pathologically, except for the evidence of syphilis. Some of these may be cases of true syringomyelia, in which syphilis has only played the part of increasing the tendency to cavitation in a predisposed nervous system.

Association of Syringomyelia with Other Conditions.—The association of spinal tumors with extensive syringomyelic cavities is not very uncommon, and in such cases it is often difficult to decide whether the syringomyelia is primary or secondary. It is often clinically silent, producing neither analgesia nor paralysis above the level of the tumor, and there is therefore no indication as to the relative ages of tumor and cavity. Yet these are true syringomyelic cavities, usually lying behind the central canal and often extending throughout the thoracic and cervical levels and even up into the medulla. The tumors associated with these extensive cavities are usually either intramedullary ependymomas or hemangioblastomas, which, although arising from the meninges, are often embedded in the spinal cord. Both these types of neoplasm are supposed to have a developmental origin. It would appear therefore that the tumor may antedate the cavitation and may give rise to it by edema or transudation. But the absence of cavitation in relation to other tumors of the same or different type with an equally long history suggests that tumor and cavity may arise independently, or with little pathogenetic relationship, on the basis of congenital malformation.

The association of syringomyelia with tumors of the brain, especially with those in the posterior cranial fossa, on which Langhans based his theory of pathogenesis, has been shown by wider experience to be no more than a chance association. While syringomyelia is not uncommonly complicated by a certain degree of hydrocephalus, which may be of a temporary character, it is difficult to trace any causal relationship between the two conditions, except in the very rare cases in which a cavity in the pons obstructs the iter of Sylvius or in cases of the Arnold-Chiari malformation. In the latter, as has been said, the cavitation in the cord is more often of hydromyelic than true syringomyelic type. Cavitation limited to the cervical cord or more extensive, although often asymptomatic, may also be found in cases of platybasia. In some such cases the cavity appears to be closely associated with the deformity of the medulla and upper cervical segments of the cord, while in others it has more of the character of a hydromyelia.

Etiology and Pathogenesis

Syringomyelia is said to be rather more common in males than in females, but this has not been the author's experience. The proportion of cases in which the first symptoms appear soon after trauma to the back appears to be greater than in other forms of spinal disease, but it is doubtful whether trauma acts as more than an adjuvant, causing more rapid progress in a disease process which is already present. Syphilis also appears to act in the same way in some cases, for example in congenital syphilis the disease may appear at an unusually early age. The fact that the symptoms often begin before the age of twenty years, and usually between twenty and thirty, suggests a developmental basis which is borne out by several anatomical characters of the disease. There is, however, little evidence of familial occurrence or hereditary transmission, the so-called familial dorso-lumbar syringomyelia being a term based on clinical evidence only and now shown (Denny-Brown, 1951) to have been used for cases with a totally different pathological basis.

Three main theories, those of developmental dyscrasia, neoplasia and edema or transudation, have been put forward in the past to account for the cavitation of the cord.

(1) According to the theory of *developmental dyscrasia*, the cavitation is due to imperfect union of the laminae of the spinal cord during

the early stages of development The supporters of this theory point to the association of syringomyelia and syringobulbia with other developmental defects of the spinal bones or cord, such as spina bifida and the Arnold Chiari malformation The central canal of the cord represents only the ventro-median extension of the cruciform canal seen at an early stage of development, and the cavitation tends to develop where the alar and basal laminae or the two alar laminae fuse This argument receives confirmation from the position of the commonest cavities in the medulla The invagination along the median raphe is clearly a congenital maldevelopment The dorso-lateral slits which pass out laterally to the nucleus hypoglossi and ambiguus separate somatic motor nuclei developed in the basal lamina, from other nuclei such as that of the descending root of the trigeminal which are developed in the alar lamina Similarly the ventral cavity in the medulla lies between the pyramidal tracts and the olives which, during development, migrate to their ventral position from the rhombic lip These developmental lines of junction may be supposed to be loci minoris resistentiae in which there is more tendency to break down under the strain of active life The lower medulla and the cervical part of the spinal cord are constantly being bent in all directions and the shearing strains, between the anterior and posterior or the two lateral halves, which thus arise will tend to break any weak tissue in the center of the cord This fact undoubtedly contributes to the special incidence of syringomyelia in these situations

(2) The theory of *neoplasia* is not so sharply differentiated from the developmental theory as may at first sight appear According to this theory the cavities result from the breaking down of neoplastic tissue For some writers this tissue may be only neoplastic in the sense that it is composed of primitive spongioblasts, while others hold that growth of tumor tissue necessarily precedes cavity formation (Weil 1945) They account for the absence of a neuroglial wall round the cavity in some cases by postulating a complete break down and disappearance of the neoplastic tissue The continued growth of the tumor might account for the frequent association of syringomyelia with gliomatous tumor of the spinal cord but the wall of the cavity and the tumor are usually of different histological types This theory may be combined with the developmental theory by supposing that the primitive or neoplastic neuroglial tissue tends to be found at the lines of fusion of the laminae in the spinal cord and medulla

(3) Langhans in 1881 drew attention to the association of syringo

myelia with tumors in the posterior cranial fossa and accounted for it by supposing that compression of the vertebral veins led to venous stasis and edema in the spinal cord with secondary disintegration of the gray matter A similar theory may be used to explain cases of cavitation of the cord above or below the level of a tumor especially a tumor of a type which tends to be cystic when it occurs in the brain Edema may also occur in inflammatory and traumatic lesions of the cord and the transuded fluid in such cases may find a path of least resistance by tracking upward or downward in the dorsal horns or the dorsal columns Such an extension is usual in hematomyelia and not uncommon in the more severe traumatic lesions of the cord A cavity thus formed would be subject to those laws which apply to cysts elsewhere and which lead to periodic increases of tension within them with consequent enlargement This theory is only applicable to cavitation in the spinal cord It does not appear to explain the very constant site of the cavities in the medulla and would be inapplicable to those cavities which are in free communication with the 4th ventricle

It is possible that all three theories have elements of truth in them Whereas the position of the cavities in the medulla argues in favor of a developmental origin it is doubtful if they are present at birth or if present what form they assume at that age While there is little evidence that true syringomyelic cavities result from the breakdown of tumor tissue the association of spinal tumors with syringomyelia is too common to be fortuitous suggesting that both are parts of a congenital dyscrasia We can only speculate as to the nature of the inherent weakness *of the central tissues of the spinal cord which makes them tend to* break down under the stress of active life, but the constant flexion and rotation to which the cord is subjected especially in its cervical part may as has been suggested play some part in causing this weakness to show itself

It has often been observed that the wall of a syringomyelic cavity may be relatively poor in neuroglial fibers but on the other hand it may consist of a dense concentric band of fibrous neuroglia These variations in the character of the wall are one of the main problems in the pathogenesis of syringomyelia In the medulla those cavities which communicate with the 4th ventricle have in general thin walls whereas in the more ventrally placed cavities the wall tends to be thicker In the spinal cord thick walled cavities are often found in cases in which the symptoms have remained static for some years Taken in conjunction

the early stages of development The supporters of this theory point to the association of syringomyelia and syringobulbia with other developmental defects of the spinal bones or cord, such as spina bifida and the Arnold-Chiari malformation The central canal of the cord represents only the ventro-median extension of the cruciform canal seen at an early stage of development, and the cavitation tends to develop where the alar and basal laminae or the two alar laminae fuse This argument receives confirmation from the position of the commonest cavities in the medulla The invagination along the median raphe is clearly a congenital maldevelopment The dorso-lateral slits which pass out laterally to the nucleus hypoglossi and ambiguus separate somatic motor nuclei developed in the basal lamina, from other nuclei, such as that of the descending root of the trigeminal which are developed in the alar lamina Similarly the ventral cavity in the medulla lies between the pyramidal tracts and the olives which, during development, migrate to their ventral position from the rhombic lip These developmental lines of junction may be supposed to be loci minoris resistentiae in which there is more tendency to break down under the strain of active life The lower medulla and the cervical part of the spinal cord are constantly being bent in all directions and the shearing strains between the anterior and posterior or the two lateral halves which thus arise will tend to break any weak tissue in the center of the cord This fact undoubtedly contributes to the special incidence of syringomyelia in these situations

(2) The theory of *neoplasia* is not so sharply differentiated from the developmental theory as may at first sight appear According to this theory the cavities result from the breaking down of neoplastic tissue For some writers this tissue may be only neoplastic in the sense that it is composed of primitive spongioblasts, while others hold that growth of tumor tissue necessarily precedes cavity formation (Weil 1945) They account for the absence of a neuroglial wall round the cavity in some cases by postulating a complete breakdown and disappearance of the neoplastic tissue The continued growth of the tumor might account for the frequent association of syringomyelia with gliomatous tumor of the spinal cord but the wall of the cavity and the tumor are usually of different histological types This theory may be combined with the developmental theory by supposing that the primitive or neoplastic neuroglial tissue tends to be found at the lines of fusion of the laminae in the spinal cord and medulla

(3) Langhans in 1881 drew attention to the association of syringo

A typical case of syringomyelia will therefore show some degree of muscular wasting in the small muscles of the hands which may show fasciculation so long as the atrophy is increasing One or more of the tendon reflexes in the arms may be reduced or absent This is often associated with some degree of paraplegia or of monoplegia of one lower limb with increased deep reflexes and plantar reflexes of the extensor type Sensory examination will show bands of analgesia or thermanesthesia without anesthesia to light touch These bands usually have a segmental distribution which may be more or less symmetrical and are most often found over the upper half of the body But departures from this rule are common On the other hand there may be segmental areas of anesthesia where all modalities of sensation are lost or in a band of sensory loss which is otherwise symmetrical the sensation of touch may be lost on one side and preserved on the other On the other hand there may be hemianalgesia and thermal loss below a certain level The lower lumbar and sacral dermatomes usually escape and may do so even in cases with very extensive sensory loss Horner s syndrome is often seen on one or both sides and is usually associated with loss of sweating over the face and neck and often also over the shoulder and arm of the affected side The skin of the affected area may be scaly and the nails brittle Other trophic symptoms are not uncommon One or both hands may be red swollen, and succulent with thin glossy skin Chronic ulcers of the hands may develop from burns cuts or other trivial causes and painless whitlows may lead to deep suppuration and necrosis with eventual loss of the terminal phalanges Alterations in the body skeleton are more often atrophic than hypertrophic and appear to result from disuse and anesthesia Thus comparatively slight injuries may cause fractures or go on to Charcot joints In contrast to tabes dorsalis the affected joints in syringomyelia are usually those of the upper limbs The spine is rarely if ever affected in this manner but kyphosis or scoliosis are common especially in cases in which the tone of the spinal musculature is altered at an age when the spinal column still retains the mobility and plasticity of youth It is doubtful whether the asymmetry in the size of the breasts or irregularities in the distribution of hair on the body which are sometimes found in cases of syringomyelia should be considered as congenital malformations or as the results of early lesions of the autonomic pathways Abnormalities of the base of the skull and upper cervical vertebrae such as platybasia assimilation of the atlas ununited transverse processes or the Klippel Feil deformity may be associated with syringo

with the characters of the walls of hydromyelic cavities at various ages, the evidence suggests that the character of the wall may depend on the conditions of tension within the cavity For example, prolonged slight stretching of the walls may stimulate fibrous gliosis, as appears to be the case in the walls of hydrocephalic ventricles, whereas more severe stretching may cause recently or imperfectly formed neuroglial tissue to break down It seems probable also that cavities which do not communicate with the subarachnoid space may be exposed to those periodic variations in tension which affect cyst cavities, wherever situated The sudden or rapid development of new symptoms and progress of old are most easily explained on these grounds Similarly, the spontaneous or surgical opening of a cavity onto the surface of the cord has been found in some cases to arrest the progress of the disease and even to ameliorate symptoms

Clinical Characters

Syringomyelia—The disease usually begins to show itself during the third decade, but in many cases the first symptoms appear before the age of 20 and cases of much later onset are not uncommon The symptoms that bring a patient to the doctor are usually those of weakness either of the lower or upper limbs but inquiry at this time will often elicit a history of sensory symptoms which may go back for many years The patient may have noticed an inability to feel pain or temperature in the hands Painless cigarette burns or whitlows may have called attention to this disability Subjective sensory symptoms such as pain numbness, or tingling usually confined to the upper half of the body, may also appear early These subjective symptoms may persist for months and pain in the distribution of one or more dermatomes may be severe and lasting The milder degrees of paresthesia are usually more transient Some degree of paraparesis usually spastic from the start, is an early symptom in many cases and may gradually increase It is rarely associated with any disturbances of sphincter control in earlier stages of the disease although this may be more severely disturbed when the patient is bed ridden The upper limbs also may be spastic but their tone is often reduced owing to severance of the reflex arc by lesions in the gray matter of the cord Wasting is most often seen in the small muscles of the hands It is often less symmetrical than in amyotrophic lateral sclerosis and almost any muscle or group of muscles in the arm or shoulder girdle may be affected

A typical case of syringomyelia will therefore show some degree of muscular wasting in the small muscles of the hands which may show fasciculation so long as the atrophy is increasing One or more of the tendon reflexes in the arms may be reduced or absent This is often associated with some degree of paraplegia or of monoplegia of one lower limb with increased deep reflexes and plantar reflexes of the extensor type Sensory examination will show bands of analgesia or thermanesthesia without anesthesia to light touch These bands usually have a segmental distribution which may be more or less symmetrical and are most often found over the upper half of the body But departures from this rule are common On the other hand there may be segmental areas of anesthesia where all modalities of sensation are lost or in a band of sensory loss which is otherwise symmetrical the sensation of touch may be lost on one side and preserved on the other On the other hand there may be hemianalgesia and thermal loss below a certain level The lower lumbar and sacral dermatomes usually escape and may do so even in cases with very extensive sensory loss Horners syndrome is often seen on one or both sides and is usually associated with loss of sweating over the face and neck and often also over the shoulder and arm of the affected side The skin of the affected area may be scaly and the nails brittle Other trophic symptoms are not uncommon One or both hands may be red swollen and succulent with thin glossy skin Chronic ulcers of the hands may develop from burns cuts or other trivial causes and painless whitlows may lead to deep suppuration and necrosis with eventual loss of the terminal phalanges Alterations in the body skeleton are more often atrophic than hypertrophic and appear to result from disuse and anesthesia Thus comparatively slight injuries may cause fractures or go on to Charcot joints In contrast to tabes dorsalis the affected joints in syringomyelia are usually those of the upper limbs The spine is rarely if ever affected in this manner but kyphosis or scoliosis are common especially in cases in which the tone of the spinal musculature is altered at an age when the spinal column still retains the mobility and plasticity of youth It is doubtful whether the asymmetry in the size of the breasts or irregularities in the distribution of hair on the body which are sometimes found in cases of syringomyelia should be considered as congenital malformations or as the results of early lesions of the autonomic pathways Abnormalities of the base of the skull and upper cervical vertebrae such as platybasia assimilation of the atlas ununited transverse processes or the Klippel Feil deformity may be associated with syringo

myelia and dolichocephaly or other abnormal configuration of the skull is sometimes described Spina bifida in the lumbar region is associated rather with hydromyelia than syringomyelia, but the close association of these two conditions has been noted

A great variety of forms of disease of the nervous system has been found on occasion associated with syringomyelia In most of these the association is probably fortuitous Cerebral tumors are now recognized to be so common that they might be expected to cause death in a small number of cases In the writer s experience this association is very rare In some other diseases the association has been assumed on clinical grounds only There is however, considerable evidence that syringo myelia may be associated with von Recklinghausen's disease, though here it is usually of limited extent Its occurrence in acromegaly also may be more than a chance combination of diseases

Syringobulbia —The symptomatology of syringobulbia is even more pleomorphic The most common sign is nystagmus on lateral deviation of the eyes Almost as common is paralysis of the muscles supplied by the nucleus ambiguus, that is the larynx pharynx, and soft palate According to Jonesco Sisesti these symptoms are present in some degree and form in 85 per cent of cases in which the medulla is involved and are bilateral in 12 per cent of these cases Paralysis of the vocal cord on the side of the lesion may be recognized only on laryngoscopic examination when the paralysis is partial affecting only the abduction of one vocal cord Even almost complete paralysis of one vocal cord may be compensated by excessive movement of the normal cord but when the paralyzed cord becomes atrophied compensation is more difficult Usually the patient notices some hoarseness of the voice, or at least a tendency for the voice to tire more quickly than before The ability to sing is lost and the speaking voice often sinks to a lower pitch than before In some cases the voice 'breaks like that of a youth varying between a high and a low pitch Alteration of the voice may come on abruptly and in such cases may improve, at least for a time by the compensatory action of the intact musculature In cases of bilateral laryngeal palsy one side is usually more affected than the other, at least in the early stages and the symptomatology is then similar to that of unilateral palsy When the abductors of the vocal cords are paralyzed on both sides there may be dyspnea which, in rare cases, has called for intubation This is due to an approximation of the vocal cords which affects inspiration more than expiration so that the speaking voice may be little altered

At a later stage when the vocal cords assume the cadaveric position the voice is lost but the patient usually suffers no other disability Paralysis of the soft palate or pharynx may show itself by difficulty in swallowing and this symptom also may be improved by a compensatory mechanism or the voice may become more nasal than before Fasciculation may be seen in the soft palate and there may be a loss of the palatal reflex on the side of the lesion Loss of taste may be found and may show a dissociation in the type of taste which is first lost Schlesinger appears to have been the first to demonstrate loss of the taste of bitter substances with preservation of that of salt sweet and sour solutions There is some evidence that the taste organs for the recognition of bitterness are more developed at the base of the tongue than in the anterior two thirds which are supplied by the pars intermedia nervi facialis and loss of this sensation is therefore likely to be found when the lower part of the gustatory nucleus or the nerves to it are damaged Loss of taste of bitter substances may progress to complete ageusia on one or both sides Atrophic palsy of the tongue is less commonly seen than paralysis of the laryngo pharyngeal musculature It is almost always unilateral On the other hand the tongue may be swollen and loll out of the mouth This probably results from the same physiological mechanism as the swelling of the hands Facial analgesia is very common It affects the eyes fore head and cheeks more commonly than the mouth area and is usually dissociated with preservation of the sensation of touch Attacks of vertigo may be an early symptom In a few cases they have been very severe and disabling but in most cases they are of slighter degree They may be brought on by alteration of the position of the head Jonesco Sisesti has found variations in the excitability of the different semi circular canals the most common being hypo excitability of the vertical canals on the side of the lesion This requires confirmation Occasionally hemiplegia is a prominent sign more often there is some difference between the deep and skin reflexes on the two sides of the body and limbs When the cavity passes into the lower pons paralysis of the muscles supplied by the facial abducens and trigeminal nerves may be present and occasionally there are other symptoms such as palatal and laryngeal nystagmus which are associated with lesions of the central tegmental tract in the pons

Relationship of Symptoms to Anatomical Lesions

It is not always easy to explain the diverse symptomatology of

syringomyelia in the light of postmortem examination, but such a study provides an interesting correlation of pathology with anatomy and physiology

The first and most obvious fact brought out by such a study is that extensive syringomyelia may exist without producing any clinical evidence of its presence This is shown best in cases in which a spinal tumor is present at the thoracic level, with a cavity extending upward into the cervical segments, here a careful physical examination often fails to reveal any abnormality above the segmental level of the tumor Similarly syringomyelic cavities found in cases dying of cerebral tumor may be completely silent The dissociated anesthesia, which is the most characteristic symptom of the disease is explained by a lesion of the fibers forming the spino-thalamic tract, with sparing of those passing up in the dorsal columns of the cord This interruption may occur at any of three positions (1) Symmetrical bands of analgesia are most easily explained by lesions of the spino thalamic fibers at their decussation in the cord, and in some cases there is evidence that these bands correspond with levels in the cord at which the cavity interrupts the anterior (white) commissure, while at levels where this is intact, sensation to pain is preserved in the corresponding dermatomes This suggests that some at least of the spino-thalamic fibers cross in the white commissure (2) Bands of unilateral analgesia must be explained by lesions in the dorsal horn or passing far laterally into the lateral horn (3) Analgesia and thermanesthesia over one half of the body below a certain level may be explained by pressure on, or destruction of, one spino-thalamic tract at the cervical or medullary level Paraplegia is most often caused by lateral distension of the cavity in the cervical region, but hemiplegia and quadriplegia may be caused by slits in the lower medulla interrupting the crossing fibers of the pyramidal tract (Fig 6) Amyotrophy is due to cavities extending into the ventral cornua As these tend to destroy the more dorsally placed groups of motor neurons the more peripheral muscles are most likely to be affected Disturbances of sympathetic outflow to the head and upper limb by destruction of the intermedio-lateral tract in the uppermost thoracic segments, are shown by Horner s syndrome and by trophic changes in the skin

At the level of the medulla oblongata each of the more common positions of the cavity produces its characteristic symptomatology Interruption of the fibers of the fillet at their decussation produces characteristic defects When this interruption is complete all sensations mediated

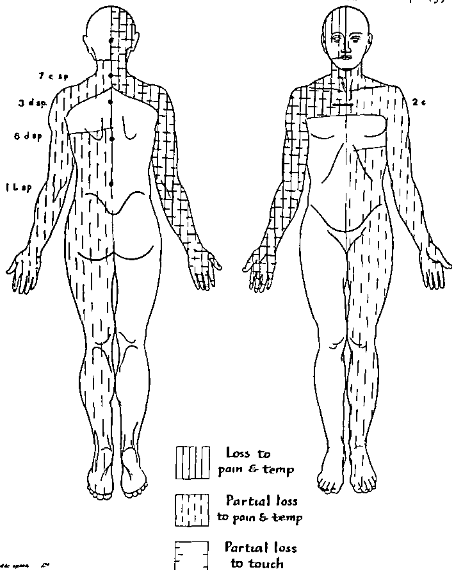


Fig 5 Sensory charts in a case of syringomyelia and syringobulbia in a woman of 66 There were coarse nystagmus on lateral deviation of the eyes wasting of the shoulder girdle muscles and biceps brachialis and spastic legs In addition to the superficial sensory loss shown on the chart there was loss of sense of position and vibration with astereognosis in the right arm

The cavity in the medulla occupied the same position as that illustrated in Fig 6 but did not extend so far laterally

by the dorsal columns on the side of the lesion disappear (Fig 5) There is loss of sense of position, astereognosis in the hand and in some cases, loss of vibration sense As the slit is usually situated low in the medulla the fibers from the nucleus gracilis alone may be interrupted in which case the symptoms will be confined to the lower limb on the same side In cases where symmetrical bands of analgesia exist over the trunk or upper limb touch will be lost along with pain and thermal sensibility on the side of the medullary lesion whereas on the opposite side of the body sensibility to light touch will be preserved The preservation of sensibility to touch elsewhere on the body below such a lesion of the fillet indicates that this modality of sensation is carried both by the spino thalamic and dorsal column fiber systems

Laterally placed cavities in the medulla also interrupt the fibers passing from the descending vestibular root to the median longitudinal fasciculus and this lesion is the most probable explanation of the nystagmus which is so constantly present

The interruption of fibers decussating from the descending trigeminal nucleus accounts for analgesia over the face and loss of the corneal reflex on the side of the lesion It is now recognized that the descending trigeminal root and nucleus correspond to the spino thalamic tracts of the cord in the modalities of sensation which they subserve, those mediated by the dorsal columns being conveyed by the main sensory nucleus and the mesencephalic root It is also believed that the fibers from the forehead and eyes pass to a lower level in the medulla than those from the mouth area which might account for the common absence of analgesia round the mouth in cases of syringobulbia Paralysis of the muscles supplied by the nucleus ambiguus has already been discussed The cavity in the medulla rarely passes as far ventrally as the nucleus itself but destroys the fibers as they swing dorsalward from it to join those coming from the dorsal vago glossopharyngeal nuclei Hemiplegia resulting from a cavity which traverses the course of the decussating pyramidal fibers in the lower medulla (Fig 6) may be an early symptom and may cause severe disability When cavitation at this level is bilateral it may produce quadriplegia

The rarer cavities which lie anteriorly between the pyramid and the inferior olive may cause atrophic palsy of the tongue by interrupting the emerging fibers of the hypoglossal nerve, or they may damage the pyramidal tract by pressure at a higher level or by destroying decussating fibers at a lower level Slits in the posterior part of the median raphe

in the medulla may produce vestibular signs and symptoms by interruption of decussating fibers from the vestibular nuclei to the medial longitudinal fasciculus but usually there is little evidence of their presence Cavities in the lower pons are often so placed as to interrupt the fibers of the sixth and seventh cranial nerves on one side

Differential Diagnosis

The diagnosis of syringomyelia may be obvious but in many less typical cases mistakes are made especially in the early stages Of the commoner diseases of the spinal cord disseminated sclerosis subacute combined degeneration amyotrophic lateral sclerosis peripheral neuropathies spinal compression by tumor or disc protrusion and syphilis may all have to be considered especially in cases in which the typical dissociated anesthesia is absent

The diagnosis of *disseminated sclerosis* is most likely to be wrongly made in cases with syringobulbia in which spastic hemiplegia or quadriplegia is associated with nystagmus on lateral deviation of the eyes and the only sensory loss in the limbs is that of position sense and two point discrimination Here the diagnosis will be helped if there is evidence of laryngeal palsy and dissociated anesthesia over the face but when the cavity is limited to the lower medulla these signs may not be evident The slow progress of the disease without remission and the absence of any change in the colloidal reactions of the cerebro spinal fluid are inconclusive pointers toward the correct diagnosis *Subacute combined degeneration* of the cord may well be considered in rare cases which come on in middle or more advanced life with paraplegia and subjective sensory symptoms and without amyotrophy The absence of any change in the blood count and the course of the disease will usually settle the diagnosis but in the early stages differentiation may be difficult *Amyotrophic lateral sclerosis* is not likely to present serious difficulty although at first sight the association of paraplegia with wasting of the small hand muscles and claw hand may suggest this diagnosis It is however unlikely that such peripheral wasting should exist in syringomyelia without any sensory loss although this may be very restricted Evidence of involvement of the sympathetic outflow to the upper limb head and neck will at once settle the diagnosis in such cases Certain types of *peripheral neuropathy*, such as that of leprosy may cause difficulty in differential diagnosis In the past considerable confusion has been caused by the use

by the dorsal columns on the side of the lesion disappear (Fig 5) There is loss of sense of position, astereognosis in the hand, and, in some cases loss of vibration sense As the slit is usually situated low in the medulla the fibers from the nucleus gracilis alone may be interrupted, in which case the symptoms will be confined to the lower limb on the same side In cases where symmetrical bands of analgesia exist over the trunk or upper limb touch will be lost along with pain and thermal sensibility on the side of the medullary lesion, whereas on the opposite side of the body sensibility to light touch will be preserved The preservation of sensibility to touch elsewhere on the body below such a lesion of the fillet indicates that this modality of sensation is carried both by the spino thalamic and dorsal column fiber systems

Laterally placed cavities in the medulla also interrupt the fibers passing from the descending vestibular root to the median longitudinal fasciculus, and this lesion is the most probable explanation of the nystagmus which is so constantly present

The interruption of fibers decussating from the descending trigeminal nucleus accounts for analgesia over the face and loss of the corneal reflex on the side of the lesion It is now recognized that the descending trigeminal root and nucleus correspond to the spino thalamic tracts of the cord in the modalities of sensation which they subserve those mediated by the dorsal columns being conveyed by the main sensory nucleus and the mesencephalic root It is also believed that the fibers from the forehead and eyes pass to a lower level in the medulla than those from the mouth area which might account for the common absence of analgesia round the mouth in cases of syringobulbia Paralysis of the muscles supplied by the nucleus ambiguus has already been discussed The cavity in the medulla rarely passes as far ventrally as the nucleus itself but destroys the fibers as they swing dorsalward from it to join those coming *from the dorsal vago glossopharyngeal nuclei* *Hemiplegia* resulting from a cavity which traverses the course of the decussating pyramidal fibers in the lower medulla (Fig 6) may be an early symptom and may cause severe disability When cavitation at this level is bilateral it may produce quadriplegia

The rarer cavities which lie anteriorly between the pyramid and the inferior olive may cause atrophic palsy of the tongue by interrupting the emerging fibers of the hypoglossal nerve, or they may damage the pyramidal tract by pressure at a higher level or by destroying decussating fibers at a lower level Slits in the posterior part of the median raphe

in the medulla may produce vestibular signs and symptoms by interruption of decussating fibers from the vestibular nuclei to the medial longitudinal fasciculus but usually there is little evidence of their presence Cavities in the lower pons are often so placed as to interrupt the fibers of the sixth and seventh cranial nerves on one side

Differential Diagnosis

The diagnosis of syringomyelia may be obvious but in many less typical cases mistakes are made especially in the early stages Of the commoner diseases of the spinal cord disseminated sclerosis subacute combined degeneration amyotrophic lateral sclerosis peripheral neuropathies spinal compression by tumor or disc protrusion and syphilis may all have to be considered especially in cases in which the typical dissociated anesthesia is absent

The diagnosis of *disseminated sclerosis* is most likely to be wrongly made in cases with syringobulbia in which spastic hemiplegia or quadriplegia is associated with nystagmus on lateral deviation of the eyes and the only sensory loss in the limbs is that of position sense and two point discrimination Here the diagnosis will be helped if there is evidence of laryngeal palsy and dissociated anesthesia over the face but when the cavity is limited to the lower medulla these signs may not be evident The slow progress of the disease without remission and the absence of any change in the colloidal reactions of the cerebro spinal fluid are inconclusive pointers toward the correct diagnosis *Subacute combined degeneration* of the cord may well be considered in rare cases which come on in middle or more advanced life with paraplegia and subjective sensory symptoms and without amyotrophy The absence of any change in the blood count and the course of the disease will usually settle the diagnosis but in the early stages differentiation may be difficult *Amyotrophic lateral sclerosis* is not likely to present serious difficulty although at first sight the association of paraplegia with wasting of the small hand muscles and claw hand may suggest this diagnosis It is however unlikely that such peripheral wasting should exist in syringomyelia without any sensory loss although this may be very restricted Evidence of involvement of the sympathetic outflow to the upper limb head and neck will at once settle the diagnosis in such cases Certain types of *peripheral neuropathy* such as that of leprosy may cause difficulty in differential diagnosis In the past considerable confusion has been caused by the use

of the name 'familial dorso-lumbar syringomyelia' for one such type This is a progressive hereditary disease in which sensation to pain is lost first in the lower limbs and later in the upper limbs, and there is a great tendency to trophic ulceration in affected areas Other modalities of sensation may be lost later The pathological basis of the disease appears to be an abiotrophy of peripheral sensory neurons (Denny Brown 1951) Differential diagnosis may be difficult in cases in which symptoms appear in early adult life, but the distribution of the analgesia will make syringomyelia unlikely Physical signs, very similar to those of syringomyelia, may be found in cases of *intra spinal tumor* or *disc protrusion* at the cervical level These, by compressing the anterior spinal artery commonly produce amyotrophy of the shoulder, limb or hand muscles and by a similar vascular mechanism or by more direct effects of pressure may interfere with the function of the pyramidal and spinothalamic tracts Disc protrusions may also cause direct pressure on the emerging roots with resulting amyotrophy and anesthesia which may be roughly symmetrical Nystagmus on lateral deviation of the eyes and Horner's syndrome are also symptoms common both to syringomyelia and to tumors at this level of the spinal cord An examination of the cerebro spinal fluid may aid the diagnosis by showing a spinal block Although the larger syringomyelic cavities may cause some lag in the rise and fall of pressure with jugular compression (Queckenstedt's test) they rarely increase the protein in the cerebro spinal fluid above the level of 100 mgm per 100 m l Myelographic studies with opaque media may clinch the diagnosis but when this remains doubtful, a laminectomy is justified both by the possibility that a removable tumor is present, and if the alternative diagnosis prove correct, by the hope that opening a syringomyelic cavity may arrest the progress of the symptoms

Spinal syphilis with amyotrophy, especially the condition called *pachymeningitis cervicalis hypertrophica*, may present an even greater problem This disease usually begins with pain in the neck or arms and progresses to paraplegia associated with amyotrophy and sensory loss in the upper limbs Gowers pointed out that in cervical pachymeningitis the anesthetic areas which involve all forms of superficial sensibility are supplied by the same spinal segments as the muscular groups which have undergone wasting The segmental representation of the anesthetic areas is usually less than that of the amyotrophy whereas in syringomyelia the converse relationship is more usual, the sensory loss often being much more extensive than the muscular wasting Pain may also be a more

prominent symptom in syphilitic pachymeningitis An examination of the cerebro spinal fluid will in most cases settle the diagnosis The Wassermann and Kahn reactions may be feeble or negative in cases of chronic syphilis but there will usually be a more complete spinal block than is found in syringomyelia

Treatment

No treatment so far tried has proved successful in more than a fraction of the cases so treated Frazier and Puusepp have reported good results from opening the cavity by surgical operation Puusepp recommends that the incision should be made into the dorsal columns in a longitudinal direction 3 mm from the midline and 1 to 3 cm in length the longer incisions being used when the pressure inside the cavity is not much raised Radiotherapy has produced some encouraging results but in other cases little improvement has been obtained The rationale of this form of treatment is far from clear and in a disease with so variable a course it is difficult to be certain that an arrest of the progress of the disease is due to the treatment Considering the probable nature of the disease process no drug treatment is likely to be of much value During episodes of rapid progress of symptoms magnesium sulphate enemata or other measures directed to reducing tension in the syringomyelic cavity by raising the osmotic pressure of the blood may be tried

BIBLIOGRAPHY

DENNY BROWN D J Neur Neuro surg and Psychiatry 1951 XIV

GOWERS W R A Manual of Diseases of the Nervous System I 3rd ed Churchill London 1899

JONESCO SISESTI N Tumeurs medullaires associees a un processus syringomyelique Masson Paris 19 9

JONESCO SISESTI N La syringobulbie Masson Paris 193

LANGHANS Ueber Hohlenbildung im Ruckenmarke in folge Blutstauung Virchow s Archiv f path etc 1885 CI 304

PUUSEPP L Chirurgische Neuropathologie II Ruckenmarke Keuger Tartu 1933

SCHLESINGER H Die Syringomyelie Deuticke Leipsig 190

TAYLOR J GREENFIELD J G and MARTIN J P Two cases of syringomyelia and syringobulbia Brain 192 XLV 3 3

WEIL A A Textbook of Neuropathology Grune and Stratton New York 1945

VII–A

Arnold Chiari Malformation

By J. Godwin Greenfield

Definition.—A deformity of the cerebellum and lower brain stem, commonly associated with spina bifida and meningomyelocele and sometimes with platybasia, assimilation of the atlas, and other deformities of the cervical spine, but also found in patients of all age groups who show no deformity of the cranium or spine.

Pathological Anatomy

The Arnold Chiari malformation consists of a prolongation of the amygdalae and adjoining parts of the cerebellum as long conical processes which pass down on either side of the dorso-lateral surface, or cover the dorsal surface of the medulla to the second, or third cervical vertebra or lower, forming an exaggerated tonsillar pressure cone. These processes usually are bound down to the medulla by connective tissue derived from the pia arachnoid. The medulla also is deformed, its posterior half being drawn downward and in severe cases forming a tongue of tissue, containing the lower end of the 4th ventricle, which overlies the dorsal surface of the upper cervical segments. The elongated 4th ventricle may reach well below the level of the foramen magnum (Figs. 1 and 2). In less pronounced cases the lower end of the medulla shows a swelling on its dorsal surface which ends abruptly in a rounded promontory limited by a transverse groove. The nerve roots issuing from the cervical segments of the cord run upward to reach their foramina of exit. The lower cranial nerves also are stretched by the elongation of the medulla. Penfield and Coburn noted in their case that the seventh and eighth cranial nerves were 5 cm. long and the ninth and tenth nerves even longer. The pons also is elongated and its ventral surface less prominent and narrower than normal, and in some cases the iter of Sylvius is also narrowed. Horizontal sections across the lower pons and upper medulla show a reduction in size which appears to affect the dorsal half more than the ventral; it is often so marked that a horizontal section through the upper third of the medulla has a smaller area than one through its lower third. The cerebellum also is generally smaller than normal and

was found by Penfield and Coburn at operation to be separated from the tentorium by a large space Several authors state that the vermis is absent but by this they only mean that the inferior vermis does not form the normal prominence in the roof of the 4th ventricle There is no

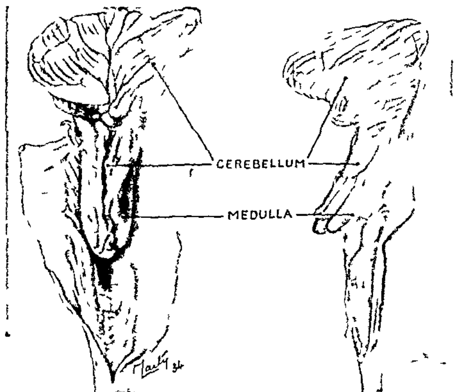


Fig 1 Dorsal and lateral views of the Arnold Chiari malformation in an infant with meningomyelocele (By the kindness of D S Russell and C Donald and the Editor of *Brain*)

demonstrable degeneration of tracts in the brain stem although abnormalities in the position of the olives have been described and there is general distortion of the medulla The cone of cerebellar tissue shows varying grades of degeneration and minor changes are seen in the cerebellum elsewhere In infants with meningomyelocele showing severe

grades of the deformity, the elongated 4th ventricle may open caudally into the spinal subarachnoid space and the cone of herniated tissue may block the flow of cerebrospinal fluid toward the intra cranial subarachnoid space (Russell and Donald, 1935) These authors suggest that operations on the sac of the meningocele in such cases may produce hydrocephalus by removing the area of absorption in the vascular wall of the

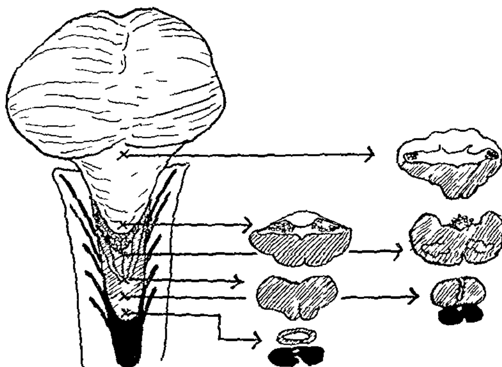


Fig 2 Diagrammatic views of the dorsal aspect and cross sections of the Arnold Chiari malformation in an infant with meningomyelocele (By the kindness of D S Russell and C Donald and the Editor of *Brain*)

sac In other cases hydrocephalus is due to congenital atresia or narrowing of the iter of Sylvius or, in older patients, to obstruction to the escape of fluid from the 4th ventricle

In older children and adults the condition is rarely seen in a severe form It may be asymmetrical or it may be associated with rotation of the lower brain stem on its long axis so that the lower cranial nerves are

stretched on one side only In many such cases there is no spina bifida or other evident causative factor in some of these cases there is an associated hydromyelia or syringomyelia

Historical Note

In a full description of a case of spina bifida Arnold in 1894 noted the deformity of the cerebellar tonsils This along with the deformity of the medulla was described more fully by Chiari in 1891 and 1895 In a series of 63 cases of hydrocephalus which he considered congenital in origin he found a deformity of the cerebellum only in 14 and of the lower medulla also in a further 7 He described two grades of the deformity (1) an elongation of the tonsils and middle part of the inferior lobe of the cerebellum as peg like processes which accompanied the medulla oblongata into the spinal canal and ( ) a displacement into a widened spinal canal of the lower parts of the cerebellum enclosing an elongated 4th ventricle He clearly distinguished this form of cerebellar protrusion from cerebellar coning due to intracranial pressure stating that he had never found it except in cases of congenital hydrocephalus Of the 14 cases of grade (1) 7 were in children ranging from 3½ months to 6 years and 7 in older patients ranging from 17 to 68 years Spina bifida was present in a child of years The more severe grade ( ) was found only in 7 young infants under 6 months suffering from spina bifida and in most cases also from meningomyelocele This relation of age group to the grade of the deformity still holds true for the great majority of cases Solovtzoff (1901) described the condition independently in infants with spina bifida Schwalbe and Gredig (1907) gave a detailed account of the pathology of the central nervous system in this condition in 4 cases of meningomyelocele The condition was introduced to English readers in 1935 by Russell and Donald who described the deformity in 10 consecutive cases of meningomyelocele All the recorded cases up to this time except the grade (1) cases of Chiari had been in infants In 1937 McConnell and Parker reported 5 cases of a similar malformation *in older children and young adults in none of whom was there any sign* of spina bifida and following this, a considerable number of non infantile cases has been published These have been reviewed by Gardner and Goodall (1950) and Sandbank (1955)

grades of the deformity, the elongated 4th ventricle may open caudally into the spinal subarachnoid space and the cone of herniated tissue may block the flow of cerebrospinal fluid toward the intra-cranial subarachnoid space (Russell and Donald, 1935) These authors suggest that operations on the sac of the meningocele in such cases may produce hydrocephalus by removing the area of absorption in the vascular wall of the

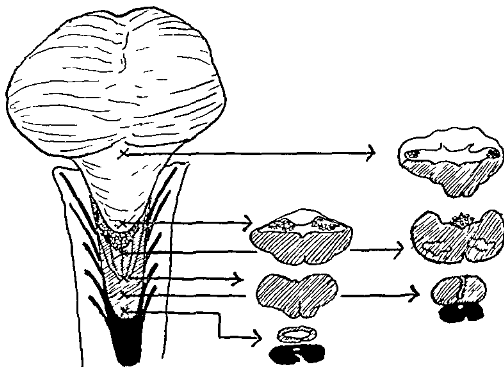


Fig ? Diagrammatic views of the dorsal aspect and cross sections of the Arnold Chiari malformation in an infant with meningomyelocele (By the kindness of D S Russell and C Donald and the Editor of *Brain*)

sac In other cases hydrocephalus is due to congenital atresia or narrowing of the iter of Sylvius or in older patients, to obstruction to the escape of fluid from the 4th ventricle

In older children and adults the condition is rarely seen in a severe form It may be asymmetrical or it may be associated with rotation of the lower brain stem on its long axis so that the lower cranial nerves are

ing adolescence e g from 15 to o in boys and at a rather younger age in girls The first symptom may be headache due to some degree of hydrocephalus or there may be loss of function of one or more of the lower cranial nerves from the sixth to the twelfth In other cases attacks of giddiness or ataxia suggest a cerebellar lesion

As the illness develops the symptomatology of a midline cerebellar tumor is closely simulated There is usually some ataxia of the limbs scanning speech or ataxic gait These symptoms may be associated with some degree of spasticity affecting all four limbs Nystagmus is commonly but not constantly present deafness which may be unilateral and is often associated with tinnitus may be an early symptom Diplopia due to weakness of one or both sixth nerves and weakness of the soft palate trapezius or tongue are often present As has already been indicated several of the lower cranial nerves on one side may be paralyzed those on the opposite side remaining intact Hydrocephalus usually indicates its presence by signs of increased intracranial pressure headache vomiting and papilledema and in some cases loss of vision from this cause has been the first symptom The symptoms have usually been present for several months and in some cases for as long as 10 years before the diagnosis is established and even at this stage they may not cause great inconvenience or danger to life They may be so slight as to be masked by those of an associated syringomyelia or platybasia It is doubtful whether it is ever possible to make a definite diagnosis of the condition in the absence of spina bifida but as the only known treatment is surgical the diagnosis of tumor of the posterior cranial fossa which is usually made leads to the correct treatment of subtentorial craniotomy

Treatment

The main difficulty the surgeon is likely to encounter when he sees the herniated tonsils and the swelling on the posterior surface of the medulla at operation is to decide whether this deformity is the cause of the symptoms or whether it is due to a more deeply situated tumor If the cerebellum is separated from the tentorium by fluid as in the case of Penfield and Coburn little doubt as to the diagnosis remains but in other cases the surgeon may be tempted to explore the cerebellum or to separate the cerebellar tonsils from the medulla Such attempts have often ended fatally and most surgeons who have experience of the condition are con

Etiology and Pathogenesis

Two theories for the development of the Arnold Chiari malformation have been advanced. According to List it is a developmental malformation beginning as early as the third week of embryonic life. Russell (1948) supports this view. Most authors, however, consider that the fixation of the spinal cord, either by the presence of a meningomyelocele or by some undetermined mechanism, prevents its ascent in the spinal canal during growth and causes traction on the medulla and lower parts of the cerebellum. When the malformation is established the space normally occupied by the cisterna magna is filled by the herniated parts of the cerebellum and medulla, and the resulting obstruction to the circulation of cerebrospinal fluid leads to hydrocephalus which may exaggerate the herniation. It seems probable that both theories have some validity. There is no clear reason why fixation of the spinal cord at the lumbar level should exert special traction effects on the medulla and brain stem, and the association of the deformity with malformations of the upper cervical vertebrae is not easily explained on the traction hypothesis. For this reason it may be premature to adopt the name 'medullo cerebellar traction displacement,' which has been suggested for this condition. On the other hand the common onset of symptoms attributable to the malformation in late adolescence, a time when elongation of the spine is still taking place but the growth of the spinal cord has almost ceased, suggests that the disproportion in the rate of growth of the spinal canal and spinal cord plays some part in the malformation if only by exaggerating a deformity which has been present from early fetal life.

Clinical Symptoms

Allusion has already been made to the very common presence of an Arnold Chiari malformation in infants with meningomyelocele and of its part in the causation of the associated hydrocephalus. Although the clinical importance of milder grades of the deformity, as seen in older patients, has been recognized only within recent years, the considerable number of cases which have been reported shows that the condition is not very rare. While most of these patients have sought advice for symptoms which are directly due to the deformity, it may also be a chance postmortem discovery in patients dying from other causes at any age.

In a large proportion of these older cases the symptoms appear dur-

ing adolescence e g from 15 to 20 in boys and at a rather younger age in girls The first symptom may be headache due to some degree of hydrocephalus or there may be loss of function of one or more of the lower cranial nerves from the sixth to the twelfth In other cases attacks of giddiness or ataxia suggest a cerebellar lesion

As the illness develops the symptomatology of a midline cerebellar tumor is closely simulated There is usually some ataxia of the limbs scanning speech or ataxic gait These symptoms may be associated with some degree of spasticity affecting all four limbs Nystagmus is commonly but not constantly present deafness which may be unilateral and is often associated with tinnitus may be an early symptom Diplopia due to weakness of one or both sixth nerves and weakness of the soft palate trapezius or tongue are often present As has already been indicated several of the lower cranial nerves on one side may be paralyzed those on the opposite side remaining intact Hydrocephalus usually indicates its presence by signs of increased intracranial pressure headache vomiting and papilledema and in some cases loss of vision from this cause has been the first symptom The symptoms have usually been present for several months and in some cases for as long as 10 years before the diagnosis is established and even at this stage they may not cause great inconvenience or danger to life They may be so slight as to be masked by those of an associated syringomyelia or platybasia It is doubtful whether it is ever possible to make a definite diagnosis of the condition in the absence of spina bifida but as the only known treatment is surgical, the diagnosis of tumor of the posterior cranial fossa which is usually made leads to the correct treatment of subtentorial craniotomy

Treatment

The main difficulty the surgeon is likely to encounter when he sees the herniated tonsils and the swelling on the posterior surface of the medulla at operation is to decide whether this deformity is the cause of the symptoms or whether it is due to a more deeply situated tumor If the cerebellum is separated from the tentorium by fluid as in the case of Penfield and Coburn little doubt as to the diagnosis remains but in other cases the surgeon may be tempted to explore the cerebellum or to separate the cerebellar tonsils from the medulla Such attempts have often ended fatally and most surgeons who have experience of the condition are con

tent to decompress the herniated mass, and open the 4th ventricle if necessary through the herniated tissue Conservative operations of this kind have resulted in complete relief of symptoms in many cases, and little appears to be gained by freeing or resecting the tongues of cerebellar tissue

BIBLIOGRAPHY

ARNOLD J Myelocyste Transposition von Gewebskeimen und Sympodie Beitrag z path Anat und allg Path 1894 XVI 1

CHIARI H Ueber Veranderungen des Kleinhirns infolge von Hydrocephalie des Grosshirns Deutsche med Wochenschr 1891 17 117

CHIARI H Über Veranderungen des Kleinhirns des Pons und der Medulla oblongata in Folge von congenitaler Hydrocephalie des Grosshirns Denkschrift Akad Wiss Wien (Math naturw Klasse) 1895 LXIII 71

GARDNER W J and GOODALL R J Arnold Chiari malformation in adults J Neurosurg 1950 7 199

LIST C F Neurologic syndromes accompanying developmental anomalies of occipital bone atlas and axis Arch Neur and Psych (Chicago) 1941 XLV 577

McCONNELL A A and PARKER H L A deformity of the hind brain associated with internal hydrocephalus Its relation to the Arnold Chiari malformation Brain 1938 LXI 415

OGRYZLO M A The Arnold Chiari malformation Arch Neur and Psych (Chicago) 194 48 30

PENFIELD W and COBURN D F Arnold Chiari malformation and its operative treatment Arch Neur and Psych (Chicago) 1938 XL 328

RUSSELL D S Observations on the pathology of hydrocephalus M R C Special Report Series No 65 H M Stationery Office London 1948

RUSSELL D S and DONALD C The mechanism of internal hydrocephalus in spina bifida Brain, 1935 LVIII 203

SANDBANK U Le syndrome d Arnold Chiari Revue Neurol 1955 83 5 9

SCHWALBE E and GREDIG M Über Entwickelungstorungen des Kleinhirns Hirnstamms und Halsmarks bei Spina Bifida Beitrag z Path Anat und z allg Path 1907 XL 132

SOLOVTZOFF N Les difformites du systeme nerveux central dans le spina bifida Nouv Icon de la Salpet 1901 14 118 & 15

VIII

Hereditary Ataxy

Under the name of hereditary or familial ataxy are gathered together several clinical types of disease which have many features in common and between which almost every variety of transitional type may be met with. The common features of these diseases may be here expressed.

Etiologically.—They tend to develop during childhood. They are hereditary and the heredity may be direct or indirect or the disease may suddenly appear among many members of the same child rank at a certain distance from a common progenitor. As with all hereditary diseases isolated cases are common in which no heredity can be traced.

Clinically.—They are characterized by a slow clumsy ataxy which in the eyes appears as nystagmus and in the speech is expressed by staccato and explosive utterance, slurring and drawling and general lack of articulatory precision. In the trunk and limbs the ataxy is shown by clumsy unsteadiness, intention tremor, titubation and by involuntary movements somewhat like those of chorea. Disturbances of sensibility, both objective and subjective, are conspicuous by their absence and the sphincters are not affected. Signs of involvement of the pyramidal system in the form of the extensor response in the plantar reflex, contractures or spasticity are present.

Pathologically.—The morbid change consists in a primary neuronic degeneration with secondary glial proliferation in the following systems: (1) in the afferent neurons comprising the posterior columns of the spinal cord; (2) in the neurons of the direct cerebellar tract and of Gowers' tract; (3) in the neurons of the cerebellum and its direct connections; (4) in the neurons of the pyramidal systems in the ascending frontal convolutions; (5) in the neurons of the retina. While all these morbid changes may coexist in the same case, yet it is common for the degeneration to fall heavily upon some of these systems while others relatively or entirely escape. For example, in the spinal form of Friedreich's disease the degeneration is practically confined to the posterior columns and the spinal cerebellar tracts, whereas in the type of primary progressive cerebellar ataxy *the degeneration is entirely confined to the cerebellum*. And again in familial spastic paralysis the lesion is confined to the pyramidal system. All such pure types are rare but combinations of these types make up the clinical and pathological entities of hereditary ataxy. Optic atrophy from

degeneration of the retinal neurons is especially characteristic of Marie's ataxy but it may occur in every other form of hereditary ataxy Not very uncommonly combinations of hereditary ataxy with other familial diseases are met with, namely, with the muscular dystrophies, with peroneal atrophy and with myotonus

The following types of hereditary ataxy are sufficiently distinct as to merit separate description and with them is included familial spastic paralysis as this latter condition seems naturally to complete a clinical and pathological series (1) Friedreich's ataxy, (2) Marie's ataxy (3) Sanger Brown's ataxy, (4) primary progressive cerebellar ataxy, (5) a type closely resembling disseminate sclerosis but familial in incidence (6) familial spastic paralysis

Many types exist which do not quite correspond with the usual descriptions of the above types and any transition between these types may exist They may show striking peculiarities in the age incidence in the clinical aspect and in the course and prognosis of the malady It is usual for the type to remain constant in the same family but even to this rule there are notable exceptions which prove the close relationship of these diseases For example, in one family which came under my observation five children were affected and of these four were very typical cases of Friedreich's disease but the fifth was a typical example of Marie's ataxy

Friedreich's Ataxy

In addition to the slow clumsy ataxy, Friedreich's type is characterized by the absence of the knee jerk and other deep reflexes by the presence of the extensor plantar response and of contractures, especially in the form of pes cavus and by the presence of curvature of the spine in the later stages of the disease

Etiology —The first signs of the disease usually appear in early childhood and before the sixth year but symptoms may not be evident until a few years later In a considerable number of cases, however the onset is delayed until the time of puberty, which in a few examples the onset may be delayed until after the age of thirty years As a rule the age incidence is approximately the same in each child rank of the same family but sometimes the phenomenon of anticipation is well marked the disease appearing at an earlier age in each succeeding generation as a whole or in successive children of the same parents

The disease is said to be slightly more common in males Isolated cases

in which no heredity can be traced are not rare but the tendency to familial incidence is striking and characteristic Indirect heredity is the most common for the reason that the subjects of this disease are usually afflicted in childhood and incapacitated by the time adult life is reached and that they therefore do not procreate Transmission occurs both through the males and through the females Direct heredity is however by no means so uncommon as has been supposed and in one family under my observation the disease had been transmitted from father to son for seven generations

Little is known concerning any other definite factors in the causation of the disease Friedreich and others have pointed out that a history of parental alcoholism is unduly common and congenital syphilis has been adduced as a possible etiological factor In the writer s experience neither alcoholism nor syphilis is in true causal relation with the disease the transmission of which through many generations directly negatives such an hypothesis Gowers considered that the malady was of an abiotrophic nature He thought that the nerve elements which degenerate were hereditarily endowed with a much shortened period of vitality after which they underwent a natural process of decay

Bing and Edinger consider that an Ersatz Theorie accounts for the degeneration Portions of the nervous system which do not receive adequate nutrition or which are underdeveloped and thus not normally resistant degenerate under the stress of relative or absolute overwork In this connection it may be pointed out that the spinal cord in Friedreich s disease may be congenitally small and the posterior roots never properly developed Newton Pitt calls attention to an inherited tendency to general early vascular degeneration as a factor but in this connection it must be pointed out that vascular degeneration is the constant accompaniment of every sclerosis following degeneration within the nervous system Lastly the possibility of a deprivative degeneration in certain nerve elements as the result of internal secretory failure must not be forgotten as the possible essential factor of this disease In more than one family under the writer s observation the disease after progressing for a few years came invariably to a final arrest thus proving that the cause of the disease in these cases had ceased to act

Morbid Anatomy—The spinal cord is unusually small Apparently this smallness may be congenital and the posterior roots tend to be small gray and poorly myelinated The essential change is a primary degeneration of certain neurons in the dorsal column of the spinal cord of the pyramidal tracts and of the spinocerebellar tracts both dorsal and ventral This degeneration commences first in the periphery of the axon which slowly dies back toward the nutrient nerve cell as the branches of an aged tree tend to die back towards the trunk

The degeneration of the dorsal columns is usually the earliest change and remains the most prominent feature throughout and it affects chiefly the exogenous fibers In the lumbosacral region degeneration is found in the whole of the dorsal columns except the cornu commissural zone and the fibers in the immediate vicinity of the dorsal horn but a certain proportion of the fibers of every region remain intact throughout the whole course of the disease In the upper dorsal and cervical regions (Fig 3) Burdach s column is usually less affected than is Goll s column but sometimes the reverse condition may obtain Lissauer s area is sometimes degenerate There is considerable degeneration of the collaterals to the ventral horns



FIG 3 —Section of the cervical spinal cord from a case of Friedreich s disease Stained by the Weigert Pal method Degeneration is conspicuous in the posterior columns and in the pyramidal tracts both cro d and direct and in the cerebellar tracts and th shrinking in size of the posterior part of the cord is striking From a photograph by Dr Greenfield

and especially of those to Clarke s column Alterations in the root ganglia are rare and insignificant The degeneration of the fibers of the pyramidal tracts appears later It has its origin in the ascending frontal convolutions where atrophy and disappearance of the giant pyramidal cells have been shown But as the degeneration is a process of dying back towards the center it is always best marked in the lower part of the spinal cord and is often not to be traced above the decussation of the pyramids

The spino cerebellar tracts are constantly degenerated the direct cerebellar tract being the most seriously involved The cells of Clarke s column from which the direct cerebellar tract takes origin and around which the pyramidal tracts end degenerate and disappear as does also the network of collaterals which surrounds these cells Consequent upon these degenerations and secondary to them well marked neuroglia proliferation or sclero i occurs and this is most marked where the degeneration is most severe u u

ally in the dorsal columns where it may be in such great excess and arranged in such irregular whorls that it was formerly regarded as the primary pathological change The cerebellum may be normal or it may show varying degrees of atrophy of Purkinje s cells or of any other of its cell elements and of the tracts connected therewith

Symptomatology —The onset is always insidious and physical signs of abnormality usually precede any complaint on the part of the patient or his relatives The first symptoms generally appear between the sixth and the tenth year of childhood but if a careful examination be made of the younger members of families upon which Friedreich s disease is incident physical signs of the disease especially an extensor response in the plantar reflex the retraction of the great toe and some degree of pes cavus may often be found before the sixth year Not infrequently the onset of symptoms does not occur until puberty and in some families it is delayed until after the age of thirty years

Ataxy is always the first symptom to appear and this is shown by an awkwardness of gait and a tendency to stumble and fall readily Sometimes it is obvious from the history that the ataxy dates from the earliest years of infancy when it is said that the child was never strong on his legs from the time of learning to walk and that he could never run properly or join on equal terms with other children at play As the disease progresses the gait slowly becomes more irregular and clumsy and acquires a reeling and staggering character which resembles somewhat that of an inebriated person The patient walks with his feet upon a broad base and staggers and reels from side to side but notwithstanding this he keeps a fairly direct line of progression He takes short steps which are unequal and also irregular in relation to the line of progression and the movement of each foot as it is raised is poorly coordinated There is never the undue excursion and noisy stamping of the feet which is so characteristic of the gait of tabetic patients The incoordination of both legs and trunk becomes very obvious in turning quickly or in rising quickly from a seat On account of the important effect of incoordination of the trunk upon the gait the ataxy of the lower limbs which is so marked on walking becomes less evident in movements of the legs performed when the patient is lying in bed

Static ataxy is very marked and this results from defective coordination of the muscles required to maintain a fixed position against external forces and especially the force of gravity Thus in standing the body oscillates from side to side in slow and clumsy fashion and coarse tremors of the head and trunk are constant features in advanced cases (titubation) There is consequently considerable difficulty in balancing the trunk upon the feet in standing Sometimes Romberg s sign is present but this is never so well marked as it is in tabes and it is frequently entirely absent

The ataxy invades the upper extremities as a rule later than the legs There is first clumsiness with the finer movements and then little by little with all the movements It closely resembles the ataxy due to gross disease of the cerebellum and differs from that which occurs in tabes in that irregular breaking of a movement towards the end of its accomplishment which has been long termed intention tremor is frequently seen

Very characteristic of the disease and highly important in diagnosis is the occurrence of irregular involuntary movements which are often described as like those of chorea or of myoclonus They differ entirely however from the movements of chorea, etc in that they occur only when the limb or some of its segments are unsupported for they depend upon a loss of synergy between the muscles which maintain the postural tone In advanced cases such movements are constantly seen in the head and neck as nodding movements and tremors and in the trunk as swaying instability when the patient is sitting unsupported or standing Similar ataxy and irregular movements affect the muscles of the eyes of the face tongue larynx etc and the respiratory muscles In the eyes they are seen as fine regular nystagmus and as coarse irregular jerkings chiefly upon lateral deviation There is no other disease in which ataxy of the facial muscles is so conspicuous for on engaging the patient in conversation all the facial muscles may be observed in irregular contraction Perhaps some of the spontaneous involuntary movements of the face are truly choreic in nature and are indicative of involvement of the corpus striatum

The ataxy of these muscles causes an invariable impairment of articulation which gradually becomes indistinct and clumsy drawling and slurred The syllables tend to be sometimes separated adding a staccato element Explosive utterance is almost constant and from the irregularity of the respiratory movements short inspiratory whoops are not uncommon Articulation thus closely resembles that of advanced disseminate sclerosis the cause being identical in the two diseases namely interference with the cerebellar coordinatory mechanism of speech It is however slower and more clumsy in Friedreich s disease than in disseminate sclerosis

The strength of movements is at first little impaired but as the disease advances and the pyramidal degeneration increases the power is gradually lost in proportion to the degree of the pyramidal degeneration which varies greatly in different cases The lower extremities are affected first and most later the arms and in severe cases at a late stage paralysis may be almost universal The muscles do not waste but in a few rare instances local symmetrical atrophy of the muscles of the feet and lower legs and of the intrinsic muscles of the hands has been reported and I have had two such cases under my care It seems probable that these cases are in reality combinations of Friedreich s disease with peroneal atrophy

The condition of the muscular tone depends upon the relative degree of degeneration in the posterior roots and in the pyramidal tracts respectively the former tending to abolish and the latter to increase the muscular tone As a rule the influence of the posterior root degeneration is preponderant and, therefore the limbs are flaccid and hypotonic but occasionally they are somewhat rigid Contractures are the rule but these are confined to the lower extremities The most constant of these produces the deformity of the feet characteristic of Friedreich s disease and known as pes cavus The great toe is strongly retracted the tarsus is pulled up the metatarsus is dropped and the plantar arch is increased The outline of the inner border of the foot comes to resemble the letter Z the tarsus metatarsus and great toe forming the three limbs of the Z This condition often reaches such an extreme degree that the foot is much shortened and the heads of the metatarsal bones and phalanges alone come in contact with the ground in the attempt to walk Some degree of flexor contracture is often met with at the knee and hip joints The fingers also are sometimes found to be over extended at the metacarpophalangeal joints

Sensibility is but little affected but in most cases minute examination reveals slight relative loss to touch pain and temperature most marked at the periphery of the limbs and diminishing upwards Similarly there may be slight loss of sense of position in the limbs with diminution of osseous sensibility to a slowly vibrating tuning fork Subjective sensory disturbances are usually absent throughout the course of the disease but tingling and numbness cramp like pains and even severe lightning pains have occurred in verified cases A girdle sensation has also been reported

The ocular movements are almost always intact apart from the already described nystagmus In rare instances strabismus diplopia and ptosis have been recorded In one family which came under my observation extreme slowness of the ocular movements occurred in three generations all of whom were observed at the National Hospital The pupils are not affected Optic atrophy is a rare phenomenon in Friedreich s disease yet it has been reported in quite a number of otherwise typical cases

Mental symptoms are usually not conspicuous but some of the patients are of poor mentality from the first while others show a tendency to severe mental degeneration in the later stages of the disease Emotional instability irritability and outbursts of temper may occur The sphincters usually escape

Absence of the tendon reflexes is a most characteristic feature and is often the first objective sign of the disease When one considers however that the absence or presence of the tendon reflexes depends upon the relative degree of affection of the posterior roots upon the one hand and upon the pyramidal degeneration upon the other it is not surprising to find in cases

where there is a major degeneration of the pyramidal tracts that the knee jerks may persist or even be brisk up to advanced stages of the disease. The abdominal reflexes gradually disappear. The plantar reflex is invariably an extensor response. The cerebrospinal fluid presents no abnormality as regards cytology, albumin content or sugar reaction.

Spinal curvature is very common and may reach a severe degree. It consists of a scoliosis of the dorsal region often with some kyphosis and with a compensatory reverse lumbar curve. The cause of this deformity is probably the defect in the postural tone of the muscles which occurs when the afferents subserving the function of postural tone which are contained in the spino-cerebellar tracts are severed.

Complications.—Friedreich's disease may be combined with a primary muscular dystrophy. Ghilarducci has recorded twenty five cases in five generations of one family. Baumlin has recorded a case of a combination with pseudohypertrophic muscular dystrophy in which the histology of the muscle was typical and the characteristic changes of Friedreich's disease were found in the spinal cord by Bing. A brother of this patient had typical Friedreich's disease. Kollarits has also recorded a case of this combination verified by autopsy. Friedreich's disease may also be complicated with peroneal atrophy or with myotonia atrophica. Examples of both of these combinations have come under my observation.

Diagnosis.—In uncomplicated cases the diagnosis is a matter of no great difficulty on account of the strikingly distinct nature of the symptoms. Friedreich's disease can hardly be mistaken for tabes since the history of heredity, the peculiar deformity of the feet and spine, the extensor response, the speech affection and the nature of the ataxy *contrast strongly* with the loss of pain sensibility and of deep sensibility, the pupillary changes, the sphincter trouble, the abnormal Wassermann reactions and the abnormal cytology of the cerebrospinal fluid in tabes. The distinction from disseminate sclerosis presents more difficulty but in this disease the onset never occurs in childhood, there is no heredity, the deep reflexes are never lost and spinal deformity does not occur.

Course and Prognosis.—The course of the disease is usually progressive in slow and irregular fashion and the prognosis is therefore in every case serious but the average duration of the disease is over thirty years and in some cases it seems to have no tendency to shorten life. The prognosis is worse and the course more rapid in those patients who have shown disability from the time of learning to walk. In some cases the disease appears to become arrested as, for example, in one family which came under my observation, twelve members in three generations were affected with typical Friedreich's disease, yet none of them was incapacitated from following a normal life and those that were deceased had all survived the

age of seventy years Similar examples have been recorded by Gowers Intercurrent maladies febrile illnesses and debilitating influences generally may have a strong effect in hastening the advance of the disease and bringing about a fatal termination Confinement to bed from any cause whatever has a most derogatory influence upon the ataxy and upon the capacity for walking It is not an uncommon experience for a patient who i able to get about in comfort to be put to bed either for purposes of examination or treatment or for illness and to permanently lose his power of walking from this temporary deprivation of his usual exercise It is therefore of great importance that these patients shall be kept off their legs as little as is possible Cases in which the ataxy becomes extreme or in which paralysis from pyramidal degeneration becomes severe neces arily become bedridden and in this condition the patients may survive for many years Coincident valvular and myocardial heart disea e not infrequently causes sudden collap e and death from cardiac failure In other cases rapid increase of the symptoms of degeneration within the nervous system is followed immediately by drowsiness asthenia and coma and death occurs in that peculiar toxic state which is commonly the end result of all degenerative nervous diseases Generally speaking the course of the disease in other previously affected members of a family may be relied upon to give reliable prognostic indications in any given case

Treatment —No treatment is known which specifically affects the malady General tonic treatment and all measures which improve the general health and mental well being often have a surprising effect in improving the ataxy Re educational training of the limbs and trunk in the form of Fraenkel s exercises are most beneficial Properly designed boots to ensure the most advantageous use of the deformed feet must be provided

Marie s Ataxy

Under the name hereditary cerebellar ataxy Marie in 1893 grouped together as a separate type certain cases which so far as the nystagmus speech and ataxy were concerned exactly resembled cases of Friedreich s disease but which were characterized clinically by spasticity of the legs with an invariable increase of the knee jerk etc and by the common occurrence of optic atrophy and by the occasional presence of the Argyll Robertson pupil He showed that the incidence of the disease is at a later age than that of Friedreich s disease He contended that the fundamental lesion causing this morbid entity was a progressive atrophy of the cerebellum and that the spinal cord in the e cases was either normal or presented minor lesions only

Cases exactly corresponding to Marie s type are not uncommonly seen

It is certain on the one hand that the pathological anatomy of these cases is not confined mainly to the cerebellum as Marie argued but that it closely resembles the pathological anatomy of Friedreich s type And on the other hand it is equally certain that both Friedreich s type and Marie s type may occur in members of the same family, since I have had under my care five children of the same parents of whom four were characteristic of Friedreich s type while the fifth was equally characteristic of Marie s type It has been further contended that an onset in later years and after puberty occurs in this type but while this may be the rule, some of the cases show symptoms from the first years of childhood

Sanger Brown s Ataxy

This type, which is now commonly called spinocerebellar ataxy " is characterized anatomically by an outstanding primary degeneration of the spinocerebellar tracts Degeneration in the dorsal columns is present but in less degree The pyramidal tract is usually unaffected The general clinical aspect of this type as regards the slow, clumsy ataxy the speech defects and the involuntary movements, is exactly the same as in Friedreich s disease The distinguishing features of the type are as follows (1) the onset of the disease occurs after puberty and may be delayed until late in life In Sanger Brown s twenty five cases in five generations of one family the onset was between the seventeenth and the thirty fifth year In Neff s thirteen cases in four generations the onset always occurred about the age of sixty years (2) Nystagmus is usually absent (3) Ptosis diplopia and extensive ocular paralysis may occur (4) Optic atrophy is the rule (5) Scoliosis does not occur The plantar reflexes are of the flexor type

Primary Progressive Cerebellar Ataxy

In this type the characteristic pathological lesion is a degeneration of the cells of the cortex of the cerebellum and of the fibers which connect this with the central nuclei The efferent cerebellar tracts are intact as are also the afferent cerebellar tracts with the exception of the olivo-cerebellar fibers which are markedly affected The whole cerebellum becomes remarkably reduced in size Gordon Holmes Raymond Lhermitte and Stelzner have all recorded families in which this disease occurred in several generations Its connection with other forms of hereditary ataxy is shown by the facts that Menzel Perrero Bing and Thomas have recorded a similar condition of primary degeneration of the cerebellar cortex in cases of Friedreich s disease in which the characteristic spinal lesions of Friedreich s disease were present Clinically this type is distinguished by the onset of

ataxy of a cerebellar type shortly after middle life but sometimes earlier Nystagmus affection of speech ataxy and spontaneous involuntary move ments closely resembling those of Friedreich s type dominate the clinical picture Optic atrophy sometimes occurs The reflexes are normal and scoliosis and other deformities do not occur The course of the disease is slowly progressive

Type of Dejerine and Thomas Olivo ponto cerebellar Atrophy

This malady which shows many features in common with primary progressive cerebellar atrophy was first described by Dejerine and Thomas who showed that the pathological lesions consist in atrophy of the cerebellar cortex and of the bulbar olivary bodies and of the gray substance and nuclei of the pons while the middle peduncles of the cerebellum are completely degenerated and the inferior peduncles partly degenerated This disease is neither familial nor hereditary but it is here described on account of the similarity of its pathological and clinical features to the other types of hereditary ataxy It commences late in life and usually in the sixth decade with clumsy ataxy of the limbs marked ataxy of speech intention tremors and spontaneous involuntary movements Nystagmus may be well marked or it may be absent The reflexes are unaffected The malady is a pro gressive one

The Type Resembling Disseminate Sclerosis

In this condition the symptomatology of disseminate sclerosis is closely imitated and most of the cases which have been recorded have been de scribed as familial cases of disseminate sclerosis as for example by Eich horst Several cases from a family in which three generations were affected were shown by me before the International Medical Congress in London in 1913 The onset in my cases has been in early adult life with a few excep tions in which onset occurred in childhood The clinical picture has been one of nystagmus ataxy of speech ataxy with intention tremors of the upper extremities with spastic ataxy of the lower extremities an exten or response in the plantar reflex and sphincter trouble The retrobulbar neuritis and the exacerbations and remissions in the symptoms which are so characteristic of disseminate sclerosis have not been noticed in these cases

In some of the families which I have observed sphincter trouble loss of the abdominal reflexes and the extensor response in the plantar reflex have been entirely absent throughout thus contrasting strongly with di seminate sclerosis and coming somewhat to resemble the type of Déjerine and Thomas and that of primary cerebellar ataxy When one considers that

the elements of the nervous system which may be affected in the degener ation of hereditary ataxy are precisely those which are commonly affected in the lesions of disseminate sclerosis, it is not surprising that the clinical picture of the latter disease may be in some cases closely simulated by the former

Familial Spastic Paralysis

This malady is here described with the hereditary ataxies since it seems to fall naturally into the group of diseases in which primary degeneration of the pyramidal tracts is a usual anatomical feature and of which a familial and hereditary incidence is the rule Moreover among the hereditary ataxies every grade of transition is seen to the type of pure familial spastic paraplegia Whilst in the majority of the hereditary ataxies cerebellar spinal and cerebral lesions coexist yet there are the purely cerebellar type the purely spinal type whilst the purely cerebral type in the form of familial spastic paralysis forms a natural end to the series The disease was first described by Erb and subsequently by Newmark in America and by Gee and Tooth in England

The disease is sometimes hereditary but is more commonly familial and incident upon several children of the same parents Sporadic cases are not very rare The onset is gradual in early life and usually occurs after the sixth year

The pathological changes consist in a primary degeneration of the pyram idal neurons which apparently takes place in proportion to their length those supplying the lumbosacral region being lower and longer are earliest affected those supplying the brain stem being shortest are the last to be affected Degenerative changes in the neurons of the posterior columns of the spinal cord are often present showing the transition to the pathological type of the hereditary ataxies

The clinical aspect consists in the slow development of spasticity and weakness first and most in the legs which gradually increases and progresses to the trunk and upper extremities and involves the face last and least The usual signs of pyramidal involvement are present in the loss of abdominal reflexes increased deep reflexes and extensor type of plantar reflex The malady is progressive increasing to complete paralysis In its course con tractures of the spastic muscles occur that of the foot and leg producing some degree of pes cavus while above this flexor contracture at hip and knee are met with Optic atrophy is by no means uncommon Mental symptoms do not occur in uncomplicated cases neither is epilepsy met with

In diagnosis this malady is most easily confused with cerebral diplegia but the latter disease appears much earlier so soon after birth *in fact* as defective movement in the child can be ascertained Further cerebral

diplegia is not a progressive disease in the majority of the cases and it is often associated with mental deficiency and recurring convulsions

IX

Landry's Paralysis

In the year 1859 Landry applied the name acute ascending paralysis to a case in which acute flaccid paralysis with loss of reflexes and without sensory disturbances commenced in the periphery of the lower limbs and rapidly spread upwards The arms were next involved and first at the periphery and later the trunk respiratory muscles neck and lastly the cranial muscles were involved and death occurred from respiratory failure He made a careful microscopic examination of the spinal cord with the method then at his disposal and failed to detect any morbid changes in the spinal cord He subsequently described the symptom complex which has since borne his name from an analysis of ten cases

Since this time a large number of cases has been recorded From the acute nature of the onset and from the spreading nature of the paralysis they have been described as cases of Landry's paralysis This name should be restricted to those cases of acute spreading paralysis in which disorders of sensibility and sphincter trouble are absent or little marked and in which recovery is complete if the patient survives and in which no gross lesion is found within the nervous system after death

It is important to bear in mind the fact that acute spreading paralysis may be produced by *gross lesions of the nervous system and it is most im*portant in diagnosis that these conditions should be at once distinguished from Landry's paralysis Foremost among such conditions are acute spreading myelitis and hemorrhage into the theca These are at once distinguished by the simultaneous development of sensory motor and sphincter paralysis thecal hemorrhage is further distinguished by the results of the lumbar puncture

Acute poliomyelitis may also in rare cases give rise to a spreading paralysis and cause much difficulty in diagnosis but it is invariable that some permanent paralysis remains upon recovery and further the lesions of poliomyelitis are both gross and characteristic

The majority of authors who have written upon this subject have made the attempt to separate Landry's paralysis from the group of acute toxic polyneuritis both on pathological grounds and on clinical grounds Such a separation would appear entirely to be unsupported by the evidence for in Landry's disease we are certainly dealing with an acute toxic process

which has an especial physiological selective capacity for the lower motor neurons though its action is not always quite confined to the lower motor neurons Exactly the same holds good for the majority of the conditions which are grouped together as acute toxic polyneuritis In both these conditions all the nervous pathological changes which have been discovered are confined to these lower neurons motor and sensory and are often in polyneuritis confined to the lower motor neurons The assumption that has been made that in Landry s paralysis the toxic process is incident upon the nerve cells in the spinal cord whereas in polyneuritis it is upon the peripheral part of the neuron the periphery of the nerve fiber does not rest upon any sure foundation and is unsupported by any clinical or pathological facts It is probable that in all conditions of toxic polyneuritis the poison acts upon the neuron as a whole and that the devitalizing action of the poison is first manifest at the extremities of the neuron both centralwards and distalwards and both physiologically and histologically The clinical separation of Landry s paralysis and polyneuritis is equally artificial and impossible though much stress has been laid upon the presence of disturbances of sensibility and the strictly peripheral distribution of the paralysis in polyneuritis As regards sensory disturbance this clinical feature is dependent upon the peculiar selective capacity of the poison For example in many conditions of polyneuritis sensory disturbances are conspicuous by their absence throughout as in lead neuritis and diphtheritic neuritis Further peripheral distribution is not even the rule in polyneuritis and forms in which the paralysis is as much or more proximal than peripheral in distribution are frequently seen Further the now generally accepted advent of so many poisons to the nervous system by means of the perineural lymphatics which deliver the dose locally into the nervous system to be subsequently spread within the nervous system must necessarily render the conception of peripheral distribution as an essential in polyneuritis untenable

The following description of this malady is based upon the personal observation of ten cases with four autopsies which have come under my observation at the National Hospital and at St George s Hospital

Etiology

What is known of the causation of the disease in general resembles that of acute polyneuritis very closely It affects males much more frequently than females and occurs chiefly in adult life between the ages of sixteen year and fifty four years The cases which have been reported in children were probably examples of the spreading type of poliomyelitis In many cases the patient is taken ill in the midst of good health while in others there has

been some known cause productive of a toxic state such as exposure to heat and cold specific infections of which smallpox diphtheria enteric fever influenza and cellulitis are the most important or a febrile attack of obscure nature Still more frequently it has immediately followed upon symptoms indicative of gastrointestinal toxemia

Morbid Anatomy

Slight hyperemia of the spinal cord and especially of the gray matter with a few punctiform hemorrhages is the only change noticeable upon naked eye examination Very definite histological changes are found upon microscopic examination in the anterior horn cells and in the cells of Clarke's column where any degree of change may be found from an early pericentral chromatolysis to a complete loss of the chromatin granules and eccentration of nuclei Neurophagia seems not to occur The most intense changes are found in those regions corresponding with the first appearance of the paralysis The myelin sheaths of the spinal cord often show a diffuse fatty change when examined by the Marchi method No neuroglia proliferation occurs The blood vessels are engorged but are free from mural changes The peripheral nerves show some degeneration secondary to the affection of the cells The skeletal muscles show early fatty changes The whole of the changes found in the nervous system seem to be of a completely recoverable nature and this is in line with the almost invariable clinical outcome that if the patient survives he recovers perfectly

The cerebrospinal fluid is in excess and clear In two of the cases under my care it presented no abnormality either as regards cell or albumin content In other cases there is an excess of albumin and in this respect it resembles the cerebrospinal fluid of polyneuritis which is usually albuminous and sometimes so highly so as to clot spontaneously Enlargement of the spleen and of the mesenteric glands is not uncommonly found

Bacteriology

In 1903 Buzzard in a very typical case which had been under my care isolated a micrococcus in pure culture from the blood after death and he found this same organism in the loose tissue forming the external layer of the theca Injection of this organism into a rabbit by the subdural method produced after some days a rapidly spreading paralysis and the same organism was found in the theca of the rabbit and isolated in pure culture from its blood The organism was not discovered in the spinal cord nor in the arachnoid space of either the patient or the rabbit and in neither case were there inflammatory reactions in these tissues

which has an especial physiological selective capacity for the lower motor neurons though its action is not always quite confined to the lower motor neurons Exactly the same holds good for the majority of the conditions which are grouped together as acute toxic polyneuritis" In both these conditions all the nervous pathological changes which have been discovered are confined to these lower neurons motor and sensory and are often in polyneuritis confined to the lower motor neurons The assumption that has been made that in Landry s paralysis the toxic process is incident upon the nerve cells in the spinal cord whereas in polyneuritis it is upon the peripheral part of the neuron the periphery of the nerve fiber does not rest upon any sure foundation and is unsupported by any clinical or pathological facts It is probable that, in all conditions of toxic polyneuritis the poison acts upon the neuron as a whole and that the devitalizing action of the poison is first manifest at the extremities of the neuron both centralward and distalwards and both physiologically and histologically The clinical separation of Landry s paralysis and polyneuritis is equally artificial and impossible though much stress has been laid upon the presence of disturbances of sensibility and the strictly peripheral distribution of the paralysis in polyneuritis As regards sensory disturbance this clinical feature is dependent upon the peculiar selective capacity of the poison For example in many conditions of polyneuritis sensory disturbances are conspicuous by their absence throughout as in lead neuritis and diphtheritic neuritis Further peripheral distribution is not even the rule in polyneuritis and forms in which the paralysis is as much or more proximal than peripheral *in distribution are frequently seen Further the now generally accepted* advent of so many poisons to the nervous system by means of the perineural lymphatics which deliver the dose locally into the nervous system to be subsequently spread within the nervous system must necessarily render the conception of peripheral distribution as an essential in polyneuritis untenable

The following description of this malady is based upon the personal observation of ten cases with four autopsies which have come under my observation at the National Hospital and at St George s Hospital

Etiology

What is known of the causation of the disease in general resembles that of acute polyneuritis very closely It affects males much more frequently than females and occurs chiefly in adult life between the ages of sixteen year and fifty four years The cases which have been reported in children were probably examples of the spreading type of poliomyelitis In many cases the patient is taken ill in the midst of good health while in others there has

severely that the paralysis seems to be proximal in distribution and that while no voluntary movement of any trunk muscle nor of any muscle of the proximal parts of the limbs can be called forth yet feeble movements of fingers and toes may be possible This has been a marked feature in every case of Landry's paralysis which I have examined either during the onset or during the recovery In this connection it must be remembered that this appearance may be simply a matter of gravity and the amount of weight which the feeble muscles have to lift in their contraction Lastly there are a few cases in which the onset of the paralysis is not local but is general and gradually deepening

The paralysis is of the painless flaccid type and is associated with a complete abolition of the deep and superficial reflexes in the affected area It first appeals to the patient as a tiredness and heaviness in the affected region when commencing in the legs trunk or shoulders and as a loss of the finer movements when commencing in the hands It usually takes some hours and occasionally some days to become complete Generally it advances smoothly and regularly upon the regions previously unaffected until the respiratory muscles and the muscle of the face and neck become affected when it is the usual result for respiratory failure to prove fatal Sometimes however the advance may cease for a while to be followed by a more rapid advance of the paralysis

In those cases which recover the advance of the paralysis ceases and those muscles which have been most recently affected begin to show some recovery quickly and any sign of recovery of power is of very hopeful import In one case for example which I watched through the night with an advancing paralysis the intercostal muscles failed completely swallowing became difficult and the facial muscles showed signs of increasing weakness Then the diaphragm failed and the patient was left breathing feebly with the sternomastoids and scaleni After remaining about an hour in this apparently hopeless condition it became obvious that the diaphragm had recommenced to act and this was followed within a few hours by the intercostals and within twenty four hours the facial and bulbar paralysis had disappeared This patient made a complete recovery within three months

When the disease does not prove fatal either from respiratory failure pulmonary complications or sudden syncope the paralysis ceases to spread and the patient enters upon the stage of recovery which presents many features of interest The flaccid muscles show a moderate degree of wasting within two or three weeks of the onset this wasting being much less in those cases which recover rapidly It is a general atrophy and is not limited to particular groups of muscles In rare cases though fair power is regained the muscles remain conspicuously small for life but generally the muscles recover their bulk and tone completely The paralyzed muscles retain

Clinical Aspect

The onset is in some cases abrupt with the appearance of the characteristic spreading paralysis Much more frequently the paralysis is preceded by certain premonitory symptoms which may last from a few hours to days or weeks These symptoms may consist in malaise headache lassitude insomnia anorexia constipation gastralgia vomiting and diarrhea and there is not infrequently slight elevation of temperature More characteristic still among the prodromal signs are subjective disturbances of sensibility Pains in the back and limbs are common and may be of a dull aching nature or they may be sharp and shooting in character Numbness tingling "pins and needles" and other paresthesias may occur over any part of the body and are most commonly complained of in the periphery of the limbs The muscles may be locally tender during this prodromal stage

The paralysis usually comes on quickly and smoothly but sometimes a cessation of its advance for a time is followed by a rapid exacerbation Such an exacerbation proved fatal in one of my cases weeks after the onset some considerable recovery having occurred during the interval The paralysis is usually symmetrical in the end but at its commencement and in slight cases which soon recover there may be very considerable asymmetry of distribution

As in Landry s original case it is not uncommon for the paralysis to commence in the periphery of the lower extremities to rapidly ascend and to involve the muscles in the order of their innervation from the spinal cord the trunk becoming affected before the upper extremities and the intercostal muscles before the diaphragm Such a true ascending paralysis must be due to direct spread of the toxic process within the spinal cord but it is by no means usual in Landry s paralysis for the muscular weakness may commence in any group of muscles as for example in the face neck upper extremities or trunk and when so commencing the spread of the paralysis is downwards constituting a descending type of paralysis The spread of the paralysis seems always to be in terms of the contiguous elements of the spinal cord

In Landry s paralysis as in acute polyneuritis the innervation of the respiratory muscles seems to be peculiarly resistant to the toxin for in both these diseases I have seen cases completely recover, in which the paralysis was universal and complete for a time with the exception of the respiratory muscles which retained some activity sufficiently long to outlast the height of the paralysis.

It is not uncommon to see in Landry s paralysis and in acute polyneuritis when the paralysis is widely spread and affecting trunk and limbs

severely that the paralysis seems to be proximal in distribution and that while no voluntary movement of any trunk muscle nor of any muscle of the proximal parts of the limbs can be called forth yet feeble movements of fingers and toes may be possible This has been a marked feature in every case of Landry's paralysis which I have examined either during the onset or during the recovery In this connection it must be remembered that this appearance may be simply a matter of gravity and the amount of weight which the feeble muscles have to lift in their contraction Lastly there are a few cases in which the onset of the paralysis is not local but is general and gradually deepening

The paralysis is of the painless flaccid type and is associated with a complete abolition of the deep and superficial reflexes in the affected area It first appeals to the patient as a tiredness and heaviness in the affected region when commencing in the legs trunk or shoulders and as a loss of the finer movements when commencing in the hand It usually takes some hours and occasionally some days to become complete Generally it advances smoothly and regularly upon the regions previously unaffected until the respiratory muscles and the muscles of the face and neck become affected when it is the usual result for respiratory failure to prove fatal Sometimes however the advance may cease for a while to be followed by a more rapid advance of the paralysis

In those cases which recover the advance of the paralysis ceases and those muscles which have been most recently affected begin to show some recovery quickly and any sign of recovery of power is of very hopeful import In one case for example which I watched through the night with an advancing paralysis the intercostal muscles failed completely swallowing became difficult and the facial muscles showed signs of increasing weakness Then the diaphragm failed and the patient was left breathing feebly with the sternomastoids and scaleni After remaining about an hour in this apparently hopeless condition it became obvious that the diaphragm had recommenced to act and this was followed within a few hours by the intercostals and within twenty four hours the facial and bulbar paralysis had disappeared This patient made a complete recovery within three months

When the disease does not prove fatal either from respiratory failure pulmonary complications or sudden syncope the paralysis ceases to spread and the patient enters upon the stage of recovery which presents many features of interest The flaccid muscles show a moderate degree of wasting within two or three weeks of the onset this wasting being much less in those cases which recover rapidly It is a general atrophy and is not limited to particular groups of muscles In rare cases though fair power is regained the muscles remain conspicuously small for life but generally the muscles recover their bulk and tone completely The paralyzed muscles retain

their excitability to faradism throughout though there may be some slight diminution of faradic excitability in proportion to the general wasting of the muscles Contractures and deformities do not occur

Disorders of sensibility, though usually present in some degree, are completely overshadowed in intensity by the motor paralysis which dominates the clinical picture of the disease The paræsthesiæ which have been described with the onset often persist and there may be cramp like pains Not uncommonly the muscles are tender upon deep pressure but there is never that severe degree of tenderness that is met with in some forms of peripheral neuritis as for example in alcoholic neuritis There is exceptionally blunting of sensibility most marked in the periphery, but this is never deep and it is rapidly transient

Though from the general weakness of the trunk muscles there may be some difficulty in emptying the bladder and rectum during the first few days and even retention with overflow incontinence that may require catheterization from the same cause yet these last but a few days and there is never any true paralysis of the action of these sphincters The deep and superficial reflexes disappear early, with the onset of the first signs of the paralysis in the affected regions The psychic functions remain entirely unimpaired throughout Occasionally vomiting occurs and is difficult to explain It is a sign of bad portent and in one case under my care which seemed otherwise hopeful it was conspicuous throughout and brought about a fatal issue

Prognosis

In about one half of the cases the paralysis advances until the respiratory and bulbar muscles are involved and death occurs from respiratory failure usually on the third or fourth day but sometimes not until ten days or more have elapsed In one case which came under my observation after some degree of improvement in the paralysis had been noticeable a rapid extension of the paralysis occurred in the sixth week and proved fatal So long as the paralysis is extending and especially when the respiratory and bulbar muscles are failing the prognosis is very grave The extension of the paralysis may however cease at any stage and when this occurs the prognosis at once becomes favorable even though there be considerable involvement of the respiratory and bulbar muscles Any sign of improvement in the paralysis of the muscles last affected is of the most favorable import The prognosis is best in those cases in which the paralysis nowhere becomes complete When improvement has set in it is almost invariable for the patient to make an uninterrupted and complete recovery in from a few weeks to three months

Diagnosis

The rapidly spreading character of the paralysis in Landry s disease is so striking as to necessitate distinction only from those few maladies in which a similar rapidly spreading paralysis may occur and these are acute spreading myelitis intrathecal hemorrhage acute poliomyelitis (spreading type) and acute polyneuritis Acute spreading myelitis is at once distinguished from Landry s paralysis by the severe sensory loss and sphincter paralysis which in the former condition develop *pari passu* with the motor paralysis and further if the myelitis does not involve the lumbosacral enlargement of the spinal cord an extensor plantar reflex will be met with

Similarly thecal hemorrhage is associated with severe sensory loss and sphincter disturbances It is always an ascending paralysis and the cauda equina and lowest regions of the spinal cord are first affected The nature of this lesion should be at once revealed by the results of a lumbar puncture The rare spreading form of poliomyelitis presents more difficulty in diagnosis especially in the acute stage The general symptoms and the pyrexia are apt to be more severe in poliomyelitis An onset in childhood is more suggestive of poliomyelitis than of Landry s paralysis A fairly high polymorphonuclear leukocytosis in the blood and a lymphocytosis in the cerebrospinal fluid are in favor of poliomyelitis The persistence of local atrophic palsy on convalescence is absolute evidence of poliomyelitis The distinction of Landry s paralysis from acute polyneuritis is held by the writer of this article to be entirely artificial since he argues that Landry s disease is merely a striking type of acute polyneuritis

Treatment

The patient must be placed at complete rest and the discomfort and panic which are likely to arise from the utter inability to move must be assiduously relieved by frequent changes of posture A mercurial aperient should be administered early and the bowels regularly relieved for in some cases obstinate constipation occurs The bladder should be catheterized if there is difficulty in micturition Both pain and pyrexia may be relieved by the administration of salicylates or aspirin The greatest care must be taken that the patient is adequately fed with nutritious and light food Stimulants are usually indicated

Atropin seems to have a definite effect in checking the advance of the paralysis especially when the respiratory muscles are weakening and it further tends to check accumulation of secretion within the bronchi Hexamethylenamin in ten grain doses (0 6 gm) six hourly seems to be of some value It may possibly act as a disinfectant to the respiratory and

alimentary mucous surfaces by which it is probable that the toxic agent gains access to the system. Lumbar puncture should be performed daily and the cerebrospinal fluid removed freely on each occasion. Oxygen may be administered where cyanosis occurs. When once the patient has shown signs that the malady has passed its height and that recovery is commencing little treatment is required except careful nursing and feeding. Gentle massage may then be employed.

X

PERONEAL MUSCULAR ATROPHY: CHARCOT-MARIE-TOOTH TYPE OF MUSCULAR ATROPHY

This is an absolutely distinct and peculiar form of muscular atrophy with a frequent tendency to occur in several members of the same family. It usually commences in mid childhood and, after progressing for some twenty years or less, comes to a final arrest. The atrophy always commences in the intrinsic muscles of the feet and throughout is strictly distal in distribution. The muscles of the face and trunk and the proximal muscles of the limbs are never affected. The atrophy leaves a peculiar elastic fibrosis in the affected muscles so that the incapacity caused by this disease is much less than in any other form of muscular atrophy of like degree. Sensibility is often slightly affected and there may be deep sensory loss. The essential morbid anatomy is a primary neuron atrophy of the anterior horn cells and of some of the afferent neurons in certain regions of the spinal cord.

Etiology

The disease usually commences between the fifth and the tenth year of childhood, but it may appear as late as the fourth decade of life. The cases commencing after adult life is reached are usually those in which no familial relations can be traced. Males and females are both affected and in some families the incidence of the disease falls indifferently upon the two sexes, but in other families the males alone suffer and the disease is transmitted to descendants only by the unaffected females.

Heredity plays an important part in the incidence, although isolated sporadic cases are not uncommon. The malady often occurs in families and has been traced through five generations and it may skip a generation and then reappear. Both males and females may transmit, though in some families males alone have been affected while the females alone transmit. No other causal factor is known except that the disease has made it appear

ance after acute specific fevers and especially after measles This relation is probably explained in that the postfebrile debility has exacerbated the appearance of symptoms in a disease already installed

Morbid Anatomy

The anterior horn cells of the affected regions show a slowly progressive atrophy and disappearance with corresponding atrophy of fibers in the peripheral nerve The cells of Clarke s column show signs of degeneration as do also some of the fibers of the posterior columns of the spinal cord and especially those of the posterolateral column Slight degeneration in some of the fibers of the pyramidal tract is usually found

The affected muscles show a simple atrophy of the muscle fibers indistinguishable from that seen when a motor nerve is divided There is a simple shrinking of the fibers which stain progressively more and more deeply with hematoxylin lose their striation and finally disappear Secondary fibrotic changes accompany the atrophy together with sclerosis of the arteries of the muscle

It seems quite clear that peroneal atrophy which after commencing at a definite age progresses for a certain number of years and then invariably reaches a final arrest in comparatively early life must be dependent upon some pathological process which is present only during a certain period and which disappears leaving the nervous system free from further degeneration for the rest of life It is quite possible that this pathological process may be a temporary abnormality in the action of the internal secretory organs

Clinical Aspect

Muscular atrophy always dominates the clinical picture of this malady It is always strictly distal in distribution and this feature will almost always serve to distinguish peroneal atrophy from any other form of muscular atrophy This is to say it does not affect one particular muscle but the distal ends of all the muscles below a certain level on the limb leaving the proximal ends of the muscles normal and it advances up the limb inch by inch the separation of the wasted portion of the muscle from the normal portion being always transverse to its length In other words the muscle fibers seem to waste in terms of the length of the spinal axons which supply them The wasting commences always in the intrinsic muscles of the feet and hollowness of the instep and thinness of the feet together with retraction of the toes and the difficulty which the pes cavus so produced entails in the fitting of boots first draw attention to the disease

As the process advances the lower segments of the anterior tibial pero

neal and calf muscles become affected and the limb is subsequently involved inch by inch until the lower third of the thigh is reached, at which stage the disease is invariably arrested This slow spread of the atrophy from the distal towards the proximal portion of the limb gives rise to a unique and characteristic feature in the appearance of the legs in this disease at its several stages As an example the complete atrophy of all the muscles below the middle of the leg and a well developed musculature in the upper half of the leg give rise to the inverted fat bottle" calf When the atrophy has involved the lower third of the thigh the lower end of the femur bare of muscle and covered only by skin and tendons contrasts strongly with the well developed muscles of the upper thigh and gives an appearance to the thigh which resembles an inverted champagne bottle

Some years after the atrophy has become marked in the lower extremities and in the usual run of cases just before the age of puberty the intrinsic muscles of the hands and first those of the thenar and hypothenar group begin to waste and this wasting may extend to as high as the middle of the forearm It must be borne in mind that the disease may become arrested at any period of its spread and especially that the upper extremities often escape altogether With the exception of the lower part of the thighs the proximal segments of the limbs do not become involved and the muscles of the head neck and trunk remain unaffected

The affected regions of the muscles waste absolutely and leave a very elastic and not strongly contracturing fibrous tissue The electrical excitability in the wasted regions becomes first lowered and then lost and in the earlier stages may show a mixed reaction in which there is lowering of excitability to faradism with a tendency to an inverted polar reaction Fibrillation of the muscles is an important sign It is seen only when the disease is progressing and in the muscles which are obviously wasting It is never general as in some cases of progressive muscular atrophy And since peroneal atrophy is at times advancing and at other times stationary fibrillation may be in one case conspicuous and in another never seen It disappears entirely when the progress of the malady becomes finally arrested and is therefore useful as a clinical indication of active advance of the disease Contractures always occur and from the nature of the distribution of the atrophy are necessarily confined to the feet and the hands In the feet pes cavus with retracted toes is the rule but sometimes and in some stages of the disease the feet and toes may be dropped and the feet inverted The sphincters are unaffected The ankle jerks are diminished or lost in proportion to the wasting of the calf muscles In the final arrested stage they are usually lost The knee jerk is always retained and is usually brisk The plantar reflexes are usually lost early so far as any response in the foot is concerned but some response in the upper thigh muscles upon stimulating

the plantar region often remains Pain tenderness and cramp are entirely absent Conspicuous loss of sensibility is uncommon but slight loss of deep sensibility loss of vibration sense and relative tactile loss may often be detected upon careful examination but in rarer cases all forms of sensibility may be severely affected or even entirely lost As an example of the latter condition a patient came under the writer s care in the arrested stage with complete atrophy of all the muscles below the knees He had had complete loss of all forms of sensibility below the knees Notwithstanding this complete motor and sensory lo he was able to get about upon his legs and to work guided by sensations which reached his consciousness from the articular surfaces of the lower ends of his femurs

Perforating ulcers may be met with upon the soles of the feet and are explained by the thinness of the feet and their deformity which coupled with the clumsiness of the use of the feet lead to the formation of severe corns which break down into perforating ulcers Loss of sensibility also is a factor in their production

The most striking of all the clinical features of peroneal atrophy is the comparatively slight disability which the wasting of the muscles and consequent paralysis and even the sensory lo s when present cause This i due to the peculiar quality of the fibro is which succeed the wasting The fibrosed muscles support the joints in such a condition of unchanging elastic stability as renders locomotion and other acts possible in a degree that is not met with in any other condition of muscular wasting Even when a rapid increase of wasting has cau ed great disability it is almost invariable to find that the advent of fibrosis in the course of time greatly lessens the disability Thus in a patient aged sixteen years who was unable to walk without assistance on account of the severe paralysis below the knees a lapse of four years found him able to earn a good wage working upon his feet though there was no change in the degree of paralysis during this time

Complications

Peroneal atrophy may in rare cases be associated with other progressive degenerative processes in the nervous system Thus in one family under the writer s care optic atrophy occurred in another family Friedreich disease was present and several cases have been recorded in which myopathy coexisted

Diagnosis

Peroneal atrophy in the early stages is easily confused with progressive muscular atrophy in that wasting of muscles and fibrillation are the conspicuous features The on et usually in childhood and the fact that the

feet are affected first the peculiar distal distribution and the presence of any familial incidence are important But the only distinction which is absolute is the distribution for progressive muscular atrophy may begin in childhood and peroneal atrophy may not appear till after middle life and often familial relations are absent in the latter malady In the course of time the diagnosis always becomes clear for progressive muscular atrophy never keeps to the classic distribution nor is it followed by the peculiar fibrosis which characterizes peroneal atrophy

Myotonia atrophica when commencing in the peroneal muscles may for a time closely simulate peroneal atrophy The presence of the least sign of myotonia the involvement of the face and the atrophy of the sterno mastoids will establish the diagnosis

The usual forms of myopathy are at once separated from peroneal atrophy by the distribution of the muscular weakness and wasting which in the former group of maladies is conspicuously upon the face trunk and proximal muscles of the limbs and in the latter upon the distal muscles of the limbs Peripheral neuritis is more rapid in its onset and is apt to be associated by marked sensory disturbances both objective and subjective and the paralysis is in terms of individual muscles which is not the case in peroneal atrophy

Course

The course is irregularly progressive for a number of years only and the advance of the disease ceases usually in the third decade of life Exacerba tions of the weakness are likely to be followed in every case by considerable improvement owing to the secondary fibrosis in the muscles

Prognosis

The disease has no tendency to destroy life Complete arrest always occurs There is invariably a tendency for the amount of disability to improve for the reason that the fibrosis of the paralyzed muscles which occurs in the course of time renders the affected limbs more serviceable and further that the patient learns to overcome his defects There is never any real recovery in the affected muscles

Treatment

The general health should be carefully maintained and the nutrition of the affected muscles aided by the application of massage and electricity Care must be taken on the one hand to avoid overfatigue of the affected muscles and on the other hand to ensure such regular exercise as is com

patible with their capacity. Bicycling, for example, since it employs chiefly the thigh muscles, is a better form of exercise for these patients than is walking. Under no circumstances should tenotomies be performed for the deformity of the feet, for such measures tend to destroy the effect of the conservative fibrosis so essential to the production of a useful limb in this disease. The use of any heavy mechanical supports is to be avoided above all things. Light, well fitting boots, so as to interfere as little as possible with the exercise of the damaged muscles, are essential. Light celluloid splints may be worn at night to correct the deformity of the feet in the advancing stages of the disease. Administration of thyroid gland and other polyglandular extracts has been recommended.

VI

HEMATOMYELIA

Hemorrhage into the substance of the spinal cord may occur in several forms and in widely separate clinical relations. It may occur without recognizable physical signs. It may result as a secondary event following severe damage to the spinal cord either by injury, inflammation, softening or tumor formation and is here in the relation of an exacerbator of the physical signs due to the original lesion. If the original lesion be a very severe one even massive hemorrhage may produce no addition to the clinical aspect and so remain unsuspected. *Primary hemorrhage into the spinal cord is,* however, of not very infrequent occurrence and cases of this nature constitute hematomyelia as a clinical entity.

The experiments of Goldscheider and Flatau have proved that fluids when slowly injected into any part of the transverse area of the intact spinal cord (the posterior white columns conspicuously excepted) tend always to seek the gray matter and there to take up a situation of fusiform shape, especially in the regions of the anterior horn, locally, and in the region of the posterior commissure and posterior horn at a distance. In other words the fluid when injected seeks the planes of least tissue resistance and at the level of the injection fills the region of the anterior horns, posterior horns and posterior commissure and when the amount of fluid injected is increased it spreads up and down the spinal cord in the regions of the posterior horn and posterior commissure. It may remain confined to one side or may spread across the cord and involve both sides. Injection of fluid into the posterior columns of white matter spreads up and down in those columns but does *not* break through into the gray matter on account of the tissue resistance which encloses those columns. In a similar way collections

feet are affected first the peculiar distal distribution and the presence of any familial incidence are important But the only distinction which is absolute is the distribution for progressive muscular atrophy may begin in childhood and peroneal atrophy may not appear till after middle life and often familial relations are absent in the latter malady In the course of time the diagnosis always becomes clear for progressive muscular atrophy never keeps to the classic distribution nor is it followed by the peculiar fibrosis which characterizes peroneal atrophy

Myotonia atrophica when commencing in the peroneal muscles may for a time closely simulate peroneal atrophy The presence of the least sign of myotonia the involvement of the face and the atrophy of the sterno mastoids will establish the diagnosis

The usual forms of myopathy are at once separated from peroneal atrophy by the distribution of the muscular weakness and wasting which in the former group of maladies is conspicuously upon the face trunk and proximal muscles of the limbs and in the latter upon the distal muscles of the limbs Peripheral neuritis is more rapid in its onset and is apt to be associated by marked sensory disturbances both objective and subjective and the paralysis is in terms of individual muscles which is not the case in peroneal atrophy

Course

The course is irregularly progressive for a number of years only and the advance of the disease ceases usually in the third decade of life Exacerbations of the weakness are likely to be followed in every case by considerable improvement owing to the secondary fibrosis in the muscles

Prognosis

The disease has no tendency to destroy life Complete arrest always occurs There is invariably a tendency for the amount of disability to improve for the reason that the fibrosis of the paralyzed muscles which occurs in the course of time renders the affected limbs more serviceable and further that the patient learns to overcome his defects There is never any real recovery in the affected muscles

Treatment

The general health should be carefully maintained and the nutrition of the affected muscles aided by the application of massage and electricity Care must be taken on the one hand to avoid overfatigue of the affected muscles and on the other hand to ensure such regular exercise as is com

pinal cord They are of pathological rather than of clinical interest and while the part which hemorrhage may play in the symptom complex which follows injury to the spinal cord must not be lost sight of the following difficulty in the diagnosis of hemorrhage must be considered If the clinical a pect resulting from an injury to the spinal cord be that of a lesion chiefly of the central gray matter it does not follow that the lesion is a hemorrhage for pressure upon the ventral spinal artery which supplies the gray matter may produce identical symptoms and further the discrimination between symptoms due to involvement of the anterior horns and tho e resulting from root lesions is well nigh impossible in some cases For example in a case of severe cervical paraplegia from fracture dislocation the symptoms pointed to a severe lesion of the gray matter and a diagnosis of central hemorrhage was made by mo t able observers and con equently operative treatment was dismissed as unavailing A year later the paraplegia having deepened laminectomy was performed under my direction Severe pressure was found and relieved and a complete and lasting recovery of full physical ability resulted

Secondary Hemorrhages —Bleeding may occur as a secondary process in poliomyelitis lethargic encephalitis myelitis and in softening of the spinal cord from any cause whatever In this connection it may be met with following the relief of pressure when a spinal tumor has been removed Grainger Stewart has recorded two cases in which hematomyelia was secondary to the pressure by an extradural tuberculous abscess

Primary Hemorrhage —In this group are included those cases where no cau e for the bleeding can be di covered and those in which the factors associated with the onset seem trivial and where any injury received seems inadequate to account for the result They form a triking and characteristic group to which the clinical entity of hematomyelia is in reality restricted

Etiology

Nearly all the cases occur between the ages of puberty and thirty years The sexes are equally affected The most careful investigation often fails to reveal any cause whatever for the on et Not infrequently a comparatively trivial cause seems responsible such as straining coughing lifting a heavy weight suppression of menses exposure to cold and diving into water The raising of the blood pressure during moments of intense excitement is certainly the cause of the hemorrhage in some of the cases an example of which is recorded below The instantaneous onset of the paralysis which is so striking a feature where a sudden jerk of the neck as in diving coughing etc may have been the immediate antecedent is very suggestive that an actual bruising of the cord by the sudden strain is

of blood, pus or cystic fluid occurring in disease invariably occupy the same positions and spread up and down the spinal cord and so give rise to a final clinical aspect closely resembling that of the spinal type of syringomyelia.

Massive effusions of blood into the spinal cord may be round or oval in shape and nearly as broad as long and this happens when clotting occurs rapidly after effusion and when the bleeding takes place into an area of softening caused by myelitis, thrombosis or pressure. Much more commonly they are fusiform in shape and occupy the planes of the least tissue resistance. Sometimes the blood is found distending a congenital cleft or cavity in the spinal cord and it seems clear that in many of such cases the bleeding is determined by the presence of such a cleft or cavity. It has been argued by several authorities that such a hemorrhage into a congenital cleft may set up gliosis and be the starting point of a progressive syringomyelia and this view is supported by the fact that some cases which apparently commence as cases of primary hematomyelia develop into cases of progressive syringomyelia. *On the other hand, the argument is equally* tenable that such cases were, from the first, examples of syringomyelia in which hemorrhage into the regions of gliosis or into the cavities was responsible for the first appearance of symptoms.

That congenital fissures and cavities in the spinal cord are responsible as determining factors in primary hematomyelia is suggested by the fact that hematomyelia is most common in the cervical region, where such defects are usually found, and it is proved by the pathological finding of such cavities filled with blood. But that all of the cases are not of this nature is equally clear, for the epiconus, where congenital defects of a similar nature are infinitely rare, is a very common seat for the occurrence of primary hemorrhage.

Small Hemorrhages.—These may be found scattered throughout the spinal cord after death from asphyxia, tetanus, phosphorus poisoning, any hemorrhagic disease, pernicious anemia and after many infective processes. They are especially common in subacute combined degeneration when definite pernicious anemia is present and were considered as the causes of the spinal degeneration by Lichteim and Leichtenstern, who first described the pathological *findings in the former* disease. *They are found* chiefly in the white matter and may be very numerous. In all these conditions such hemorrhages seem to be terminal events occurring very shortly before death and are not associated with any definite symptoms.

Traumatic Hemorrhages.—Since bleeding is a sequel of every severe injury, massive hemorrhages may be found in cases where gunshot and other penetrating wounds, impact lesions from missiles, bruising from the jar of high explosives or falls and fracture dislocations have injured the

The general distention of the spinal cord by the increasing hemorrhage and the edema resulting from this causes a spastic paralysis below the level of the lesion and interference with sphincter control with the usual loss of abdominal reflexes briskness of knee and ankle jerk and extensor type of plantar reflex In this early stage of the malady cystitis and bedsores may give trouble Death may occur before the bleeding has ceased from extension of the hemorrhage as high as the fourth cervical segment and consequent paralysis of the diaphragm (The intercostal muscles are usually paralyzed in cervical hematomyelia either from a downward extension of the hemorrhage which is very common or as a part of the paraplegia) Such a fatal result is however very rare for it is most unusual for the hemorrhage to extend as high as the fifth cervical segment

When the bleeding has ceased and absorption of the clot commences there is a gradual clearing up of the symptoms As the distention of the spinal cord lessens the spastic paraplegia and the sphincter trouble abate and in the course of time great improvement may occur and even complete recovery so far as the paraplegic symptoms are concerned The initial local atrophic paralysis narrows down somewhat as the local effects of the pressure and edema produced by the hemorrhage upon the ventral horns pass off leaving a permanent atrophic paralysis with vasomotor paralysis and sympathetic paralysis corresponding with the regions of the ventral horns which have been irrecoverably damaged The analgesia and therm anesthesia resulting from the local destruction of the posterior commissure remain permanently The similar sensory loss due to involvement of the crossed tract in the anterolateral region of the cord is transient or permanent according as the lesion in that region is destructive or recoverable

A few of the cases after making considerable improvement progress as do cases of syringomyelia Here the explanation is either that a hemorrhage has occurred in the lesion of a previously symptomless syringomyelia or that the irritation produced by the hemorrhage is capable of starting a central gliosis of the spinal cord The cerebrospinal fluid shows no abnormality during the first few days following the onset The hemorrhage seems never to burst into the meninges Later on the fluid may present a yellow color (xanthochromia) from the gradual discharge of the blood pigments from the clot

The following examples will serve to illustrate the clinical aspect of hematomyelia in the cervical region and in the lumbosacral regions respectively

A factory girl aged sixteen years and in perfect health was roused to a high pitch of passionate rage by the behavior of a fellow worker and made a furious attack upon her with both fists During the course of this assault she felt her hands and arms go weak and become numb Five minutes later

responsible for the lightning like onset of the paralysis and that the hemorrhage is a secondary result of such bruising, for it is difficult to conceive that a hemorrhage could produce a complete abrogation of the functions of the spinal cord in the space of one second whereas this might easily result from a slight bruise

The age incidence falls among young adults when the mobility of the spinal column the muscular development and possibility of still persistent spinal clefts are all likely to be factors in the production of hematomyelia The condition may however occur in children at any age Obviously the cases which result from severe injury to the spinal column occur at any age and are met with more often in males since this sex is more exposed to the possibility of accident Otherwise the sexes are equally affected

Clinical Aspect

Hematomyelia is characterized by sudden onset usually without any pain but commonly with a sensation of numbness "pins and needles or an electrical sensation in the region affected The paralysis may be instantaneous as from a sudden bruise of the spinal cord or rapidly ingravescent such as would result from a quickly gathering hemorrhage, the local segmental signs appearing first and the paraplegic signs subsequently The clinical aspect is that of a lesion of the central gray matter of the spinal cord There is local atrophic paralysis of the muscles supplied by the segments involved from extension of the hemorrhage into the anterior horn cell region with involvement of the sympathetic system vasomotor paralysis sweating and if the lesion is in the cervical region with cervical sympathetic paralysis in addition These signs will be unilateral bilateral or irregular according to the extent of the damage to the anterior gray matter There is bilateral loss of sensibility to pain and temperature from destruction of the posterior gray commissure in which the path for these forms of sensibility crosses The vertical extent of such loss upon the body is determined by the vertical extent of the hemorrhage in the region of the posterior commissure

There is frequently loss of sensibility to pain and temperature on the opposite side of the body below the level of the lesion when the latter is more extensive upon one side of the cord from involvement of the crossed path for pain and temperature lateral to the ventral gray horn The posterior columns are conspicuously exempt in most cases and there is consequently neither loss of touch of position nor of muscle sense There is sometimes a zone of hyperesthesia at the upper limit of the sensory loss On account of the obliquity of the crossing of the path for pain and temperature in the posterior commissure the upper limit of the sensory loss is always a few segments below the upper limit of the muscular wasting

In this case the hemorrhage permanently destroyed the ventral horns of the fourth and fifth lumbar and first and second sacral segments but left the fourth sacral segment intact

Course

Following the sudden onset and abrupt development of symptoms the hemorrhage ceases in the majority of the cases and with the gradual absorption of the clot the symptoms abate leaving the patient permanently crippled to a greater or less extent with atrophic paralysis spastic paralysis and loss of pain and temperature sensibility the degree of which varies according to the region of the spinal cord which is affected and according to the amount of permanent destruction of tissue in the affected segments During the early stages of the disease there may be danger to life in the cervical cases from interference with the respiratory muscles and later on from cystitis bedsores and pulmonary complications

Diagnosis

The diagnosis of primary hematomyelia rests upon the sudden onset the rapid development of symptoms which soon come to a standstill and the physical signs of a central lesion of the spinal cord namely local atrophic paralysis of the muscles loss of pain and temperature sensibility with a conspicuous escape of other forms of sensibility and when the lesion is above the lumbosacral enlargement spastic paraplegia from the general pressure exerted by the hemorrhage upon the structures of the spinal cord

The distinction has to be made from acute myelitis and acute polio myelitis Acute myelitis though rapid in onset does not show the sudden development of symptoms seen in hematomyelia Prodromata often precede the onset This disease is rare in the cervical and lumbar enlargements where hematomyelia is most common It usually affects the whole transverse area of the cord and therefore does not give the peculiar dissociated sensory loss It is nearly always of syphilitic origin and the Wassermann reaction in blood and cerebrospinal fluid is positive and the latter shows a lymphocytosis From acute poliomyelitis hematomyelia may be distinguished by the initial febrile symptoms of the former disease by the absence of sensory loss and by the lymphocytosis in the cerebrospinal fluid

Treatment

Absolute rest is all essential It has been often urged that the prone position or a position lying upon the side supported by pillows or by a

she was completely unable to move either upper limb below the shoulder and the upper limbs and chest felt numb though she could still feel touches. She waited for two hours until the works closed and then walked home a distance of two miles. In the course of that evening the lower extremities became completely paralyzed and control of the sphincters was lost. This condition persisted for a fortnight when she began to recover the control of the sphincters and the use of her legs and this recovery was progressive and complete. The upper limbs recovered in part leaving her with a complete atrophic paralysis of all the intrinsic muscles of the left hand, flexors of wrist and fingers and of the extensors of the fingers and with complete atrophic palsy of the intrinsic muscles of the right hand. There was vasomotor paralysis with sweating over both hands and well marked cervical sympathetic paralysis of the right side. There was complete loss of sensibility to pain and temperature over the trunk from the level of the nipples to Poupart's ligaments. There was a similar loss over the left lower limb. Sensibility in the right limb was normal.

In this case the hemorrhage involved the seventh and eighth cervical and the first dorsal segment on the right side and the eighth cervical segment on the left side. On the right side it destroyed the cervical sympathetic mechanism and the crossed path for pain and temperature sensibility, thus producing the loss to pain and temperature over the left leg. The hemorrhage extended downwards in the region of the posterior commissure as far as the lower dorsal region, thus producing the bilateral loss to pain and temperature over the trunk. The difference of level between the atrophic palsy and the sensory loss owing to the oblique crossing of the pain and temperature path was characteristic.

A kitchen maid, aged twenty years, having lit her fires early one morning sat down upon the floor and proceeded to lace up her boots in a doubled up position. While tugging at the lace she suddenly felt an electric thrill throughout her legs and hips and power and sensibility in the legs at once failed and she rolled over unable to get up. Loss of sphincter control occurred immediately. On examination she was found to have complete flaccid palsy of both lower extremities with sensory loss to pain and temperature over the segmental areas from the third lumbar area downwards. Posterior column sensibility was only slightly diminished. There was complete incontinence. In the course of time recovery occurred in the adductors of the thigh, the glutei and the quadriceps and the knee jerks returned. The sphincters also recovered, together with sensibility in the third and fourth sacral areas. Complete atrophic palsy of all the muscles below the knees and of the hamstrings persisted, together with complete loss of sensibility to pain and temperature over the fourth and fifth lumbar and first and second sacral areas, with vasomotor paralysis and sweating

emboli on the other The major capacity for fat to hold nitrogen in solution causes the liberation of nitrogen bubbles to occur most readily in the fatty tissues This liberation of gas bubble occur more easily in those parts of the body where the blood supply is less abundant and therefore the rapid return of the excess of nitrogen to the atmosphere by solution in the blood stream is made less easy For these reasons the white matter of the nervous system composed as it is of a fatty substance and particularly those parts of it which are less liberally supplied with blood such as the white matter of the lower dorsal spinal cord is the most common site of gas liberation The joints and also their surrounding structures which are poorly vascularized are also common sites of the lesions as are also the subcutaneous tissues of fat subjects on account of the high solubility of nitrogen in the fat

These phenomena occur only upon decompression and are always preventable if adequate means be adopted (1) to limit the time of exposure to very high atmospheric pressures so that high degrees of tissue saturation with nitrogen shall not occur and (2) to regulate the return to normal atmospheric pressure by graduated decompression in such a way as to prevent the boiling of nitrogen in the tissues They are curable after they have appeared by immediate recompression followed by very gradual decompression Exposure of the living animal to very high atmospheric pressures may be associated with most serious and usually fatal results which occur before decompression and which are due to oversaturation of the tissues with oxygen tissue death resulting from oxygen poisoning

Etiology

This disease made its appearance in the middle of the nineteenth century when the invention of Siebe's diving dress and of subaqueous chambers made it possible for subaquatic engineering and marine salvage to be performed under high atmospheric pressures The men work in a pressure of air which just exceeds the hydrostatic pressure of that depth of water which extend from the working position to the surface and the pressure is produced and maintained by pumps and regulating apparatus

Workmen reach the working face of the caisson by passing from the normal atmosphere through a series of chambers with airtight doors in which the air pressure is raised by rapid stages until the high pressure of the working face is reached They leave through the same chambers the air pressure being lowered for some space of time in each as they pass through This process is termed compression" and decompression or locking in and out The diver is compressed as he slowly descends by an increasing air pressure from his pump and is decompressed as he ascends much

blanket covered plank arranged vertically in the bed and against which the patient rests should be secured so that the seat of the hemorrhage may not occupy the dependent part of the trunk Such a position however must not be maintained at the expense of any respiratory embarrassment nor involve any possibility of the production of bedsores thereby Application of ice to the spine is of doubtful value

Measures should be adopted to allay panic to keep the blood pressure from temporary elevations and to check the hemorrhage Morphia calcium lactate and turpentine are the most likely to be of use in this connection Ergot in full doses and other vasoconstrictors have been advocated but it is not certain whether the increased blood pressure produced by these drugs may not more than counteract any local vasoconstrictor effect that they may have Great care must be taken from the first that no distention of the bladder shall occur for this is the primary cause of cystitis If cystitis has set in it is essential to revert to suprapubic drainage at once

The most scrupulous attention must be paid to the skin in the way of cleanliness hardening and avoidance of pressure lest bed ores should develop If lumbar puncture is requisite for diagnosis a minimal amount only of fluid should be drawn off and this should be done slowly Sub e quently the administration of mercury and of iodid of potassium may aid the absorption of the clot Belladonna in moderate doses is always useful in aiding the return of sphincter control Ultimately massage passive movements exercises and the application of supporting apparatus are to be employed as in all other cases of spinal paralysis

XII

Caisson Disease

Synonyms —Compressed air illness diver s paralysis

Caisson disease is the name given to a series of phenomena which may result in any living animal upon return to a normal atmospheric pressure after exposure to an air pressure which must exceed eighteen pounds to the square inch above mean atmospheric pressure These phenomena occur the more frequently and severely the greater the air pressure and in direct proportion to the length of time of exposure to the high air pressure and the more rapid the return to a normal atmospheric pressure They are caused by the saturation of the living tissues with nitrogen at high atmospheric pressure which on too rapid return to lower atmospheric pressures boils within the tissues and this liberation of bubbles of nitrogen within the system causes tissue disruption and destruction on the one hand and gas

by means of the blood stream is slow or in those tissues in which nitrogen is especially soluble such as the fats and myelin of the nervous system the nitrogen is liable to escape in the form of bubbles To the mechanical effects upon the tissues in which the boiling of the nitrogen occurs the symptoms of caisson disease are due

That part of the nervous system which is least vascular namely the four lower dorsal segments of the spinal cord is the most common region for the lesions to occur while the joints and peripheral nerve trunks are also often affected

Massive escape of gas may occur into the blood stream and the heart has been found distended with gas after death in rapidly fatal cases A similar escape of gas into the intestines may produce severe and even fatal abdominal distention It is doubtless one of the causes of the abdominal pain nausea and vomiting which are common symptoms of compressed air sickness

The composition of the gases which escape into the tissues after exposure to compressed air has been ascertained many times by the experimental compression of animals and in fatal human cases The liberated gases are made up of 82 per cent nitrogen 16 per cent carbon dioxide and 2 per cent oxygen

The liberation of these gases and therefore the occurrence of the compressed air disease depends directly upon these factors (1) the amount of pressure to which the living animal is exposed (2) the length of time of exposure to the high pressure and (3) the rapidity with which a return is made from the high pressure to normal atmospheric pressure For example the malady never occurs after short exposures such as fifteen minutes at a pressure of 45 lbs or two minutes at a pressure of 75 lbs even though decompression be as rapid as possible for these periods are too short to allow of nitrogen saturation of the tissues It is for this reason that compressed air sickness is so much less common in divers who for the most part work for very short times only at high pressures and so much more common in caisson workers who work for many hours at a stretch at a pressure of from 30 to 40 lbs

There is one other factor which must be carefully borne in mind and that is the amount of fat present in the body which from its nitrogen dissolving qualities greatly increases the tendency to nitrogen boiling within the tissues if it be present in large amount It has been shown experimentally that fat animals succumb to the disease while lean ones escape and experience has shown the necessity of excluding fat workmen on account of their liability to the malady

The disease is obviously always preventable firstly by shortening the periods of exposure according to the height of the pressure so as to obviate

more slowly, this compression being regulated by an automatic valve in his helmet which retains the air pressure until it exceeds that of the water pressure outside. Caissons are worked under a much lower pressure than that at which divers can work, but the working shifts are much longer, whereas the diver at great depths remains down only a very short time. Roughly speaking, each thirty three feet of water produces a pressure of fifteen pounds to the square inch (five and a half fathoms).

Caissons are usually worked at a pressure of below 35 lbs. and in six to eight hourly shifts, but they have been successfully worked at a pressure of 45 lbs. with two hourly shifts and at 50 lbs. with one hourly shifts. Divers frequently work at 20 fathoms (53 lbs.) and the record depth and pressure reached has been 210 feet (95 lbs.).

During compression no trouble is experienced beyond discomfort in the ears and rarely perforation of the membrana tympani from disparity of air pressure in the middle ear. This the workmen avoid by opening the eustachian tubes with an act of swallowing or yawning, but it must be remembered that no person suffering from eustachian catarrh should be allowed to enter the air locks. Under high atmospheric pressures combustion proceeds more readily: a candle when lighted burns away furiously and a pipe bursts into flame with each draw. The workmen find that they can work more easily and with less fatigue. During exposure of the living animal to a high atmospheric pressure the tissues become gradually more and more saturated with nitrogen, first the blood and those tissues which are well supplied with blood vessels and last those tissues which are least vascular, such as the cartilages and joint structures. The amount of nitrogen thus locally absorbed will be greatest in those tissues in which the solubility of nitrogen is greatest, namely, the fatty tissues and especially the myelin of the white matter of the central nervous system. The degree of nitrogen saturation of the tissues will depend upon the degree of atmospheric pressure and upon the length of exposure to such pressure.

The symptoms of the disease become manifest upon return to a lower atmospheric pressure and directly in proportion to the suddenness of return to such pressure. If the return to a normal atmospheric pressure from a high and prolonged pressure be sudden, there may be a liberal escape of bubbles of nitrogen gas in the blood and in the tissues. In other words, the nitrogen boils with the production of local tissue disruption and general gas embolism. The presence of the nitrogen may sometimes be felt as gas crackling underneath the skin or subcutaneous emphysema.

When the return to a normal atmospheric pressure is more gradual, the nitrogen may have time to escape from the blood and from most of the tissues by diffusion through the lungs, but in those tissues which are relatively non vascular and from which for that reason interchange of gases

Clinical Aspect

The symptoms may be first manifest during the process of decompression when the latter is rapid and from a high pressure as in the case of the Malay pearl divers who take little trouble about slow ascent and who almost invariably lose their lives in the end for this reason More often the signs of the malady appear soon after a normal pressure is reached while not infrequently they do not occur until an hour or more has elapsed In slight cases headache giddiness diplopia and faintness may occur and these symptoms pass off soon and leave no trouble Severe and important symptoms occur in the following order of frequency (1) pain in the extremities or trunk commonly called by the workmen the bends from the position in which the painful limbs are held (2) pain in the epigastrium sometimes accompanied by nausea vomiting and abdominal distention (3) paraplegic paralysis which usually involves both motor and sensory and sphincter functions and which usually extends as high as the ninth dorsal segmental level (4) headache vertigo and coma (5) sudden death (6) hemiplegia or monoplegia of cerebral origin

The pain in the limbs is of a neuralgic character and is referred to the joints which are kept in the semiflexed position any attempt to straighten them causing great pain hence the common term "the bends which is applied to this symptom The pain may come on gradually or suddenly and may be slight and transient or severe and persistent It is often intolerable The knees ankles and hips are the most frequently affected but sometimes the joints of the upper extremities or of the back and especially of the lumbar region may be affected The pain persists notwithstanding the presence of paraplegia with sensory loss

Epigastric pain is common and unless quickly relieved by recompression it is followed by nausea and vomiting Vomiting may occur without pain but this is usually of intracranial origin and associated with other signs of intracranial disturbance

The paraplegia usually has its upper limit in the lower dorsal region but it may reach the cervical region and involve the arms It comes on rapidly and involves both motor sensory and sphincter functions It may be of any degree of severity from a slight and transient effect to a complete and permanent loss of the functions of the spinal cord The paraplegia occurs with increasing frequency and completeness in proportion to the degree of pressure and the length of exposure to its influence It occurred in sixty one per cent of 119 cases in St Louis bridge caissons which were worked at plus fifty pounds of pressure and among these there were fourteen deaths

There is no general relation between the pain and the paralysis as either may occur without the other and it seems therefore that the pain is due

nitrogen saturation and secondly, by arranging that such a graduated and prolonged return to normal pressure be made as will prevent any possibility of nitrogen boiling the slow return to normal pressure allowing of the nitrogen desaturation of the tissues without bubble formation and so preventing the lesions that cause the symptoms

It is quite safe and does not produce any ill effects whatever for a man to breathe pure oxygen for as many as six hours at a time This has been proved by the use of the Siebe Gorman life saving dress for rescue work from choke damp in mines Beyond a certain limit of pressure however oxygen becomes poisonous

Highly compressed air causes rapid toxic effects in proportion to the partial pressure of the oxygen It tends to cause direct death of the tissues At lower partial pressures it has a convulsant effect and at still lower pressures produces congestion of the tissues and especially of the lungs which may present consolidation and all the signs of acute pneumonia however slowly and carefully decompression has been accomplished The limit of safety so far as oxygen poisoning is concerned is ten atmospheres or 300 feet of water Neither divers nor caisson workers ever work at anything like so high a pressure

Morbid Anatomy

The essential features are the presence of bubbles of nitrogen in the tissues or bulky collections of nitrogen within the organs as in the heart or in the intestines and the results of the associated tissue disruption and air emboli When it is considered that the mass of the blood constitutes about five per cent of that of the whole body and that the capacity of the tissues in a thin subject is thirty five times that of the blood the ratio being much higher in a fat subject since fat will dissolve five times as much nitrogen as will any other tissue the presence of bubbles in the tissues and especially in the fatty tissues will readily be understood

The bubbles form first in the venous blood and in the fatty tissues where they grow by accretion and cause tearing of the tissues while air emboli and subsequent necrosis are common Hundreds of bubbles have been counted in the spinal cord and these are much more numerous in the white matter than in the gray matter Collections of nitrogen may be found in the subcutaneous tissues and may cause palpable crackling Bubbles of gas are not uncommonly found in the liver cells Occasionally similar lesions are found in the brain or in the eye and in fact may occur in any of the tissues In every fatal case which has been adequately examined patches of necrosis in the dorsal region of the spinal cord with the usual secondary degenerations have been found

working shifts must be shortened as the pressure gets higher The shifts should be not longer than 6 to 8 hours at a pressure of 30 to 35 lbs or 3 atmospheres 2 to 3 hours at a pressure of 45 lbs and one hour only at a pressure of 50 lbs At higher pressures than this which are only encountered by divers a few minutes exposure is allowed only

Compressed air sickness never occurs if the return to the normal atmospheric pressure be sufficiently slow Animals can be exposed to very high pressures short of those causing oxygen poisoning with impunity provided they be decompressed slowly enough This decompression is carried out in the case of the diver by raising him to various levels in stages and letting him remain at each stage a longer and a longer period as the surface is approached In the case of caisson workers a series of air locked chambers is provided in which the air pressure is lowered in stages the men remaining longer and longer at each stage as they approach the normal pressure The important fact in connection with decompression is that the absolute pressure can always be halved *forthwith* without any risk In the first air lock on leaving the working face of a caisson for example the pressure is at once reduced to one half that of the working face and in the remaining air locks the pressure is reduced by stages until zero is reached

Leonard Hill has shown experimentally that it is always safe to lower the pressure to plus 20 lbs by gradual decompression during the space of ten minutes then to wait at that pressure for two hours and then bring the pressure to zero by gradual reduction in ten minutes The Admiralty rules for divers require that a diver working say at 140 feet shall be first raised straight away to a depth of 50 feet where he waits ten minutes then to 40 feet for ten minutes 30 feet for twenty minutes 20 feet for thirty minutes 10 feet for thirty five minutes and then he leaves the water abruptly The difficulty and danger is the tendency on the part of the workers to curtail these weary waits and get away from work as soon as possible It is important that all fat subjects and all those who have shown a susceptibility to compressed air sickness and all those not in absolutely sound bodily health shall be excluded from working in highly compressed air

Curative Treatment—It was early discovered by the caisson workers themselves that the only remedy for the malady was to re-enter the high air pressure A recompressing apparatus in the form of a medical air lock is now supplied at all caisson works and on all ships engaged in deep salvage On the appearance of any symptoms the worker is placed in the compressing room and the pressure is run up to the full pressure at which he has been working when it is usual for the symptoms to rapidly ameliorate or disappear After the recompression the decompression must be carried out very slowly for the bubbles once formed in the tissues are not easy to get rid of though they may be kept at a small size by the pressure

to a peripheral lesion and not to the lesions of the spinal cord It is an interesting fact that the peripheral pains may persist in severe degree even when there is total loss of pain sensibility from the spinal cord lesions Symptoms indicative of lesions in the brain and cerebellum may occur such as monoplegia hemiplegia cerebellar ataxy etc but they are not common Cutaneous ecchymosis is common

The duration of the attack may vary within very wide limits The severity of the initial symptoms and the immediate application of appropriate treatment are the all important modifying factors in the prognosis The attack may last for a few hours only or it may continue for days The paralysis may recover in a few days or it may last for months and may never recover Death occurs only in cases which have severe initial symptoms and except when occasioned by complications such as cystitis and bedsores it usually takes place shortly after the attack

The following description of a typical fatal case from too long exposure to heavy pressure too rapid decompression and absence of treatment by recompression is worthy of note A diver of strong physique and in good health descended to a depth of twenty four and a half fathoms in search of a torpedo and remained at this pressure of plus sixty five pounds for forty minutes He was drawn up much too quickly and was allowed to reach the surface in twenty minutes He remained perfectly well for eight minutes when he complained of sudden pain in the stomach and immediately after became unconscious and cyanosed with stertorous breathing He died fifteen minutes after reaching the surface or some seven minutes from the time of his first symptom At the necropsy the blood vessels throughout the body were beaded with gas bubbles and the liver frothed on section The heart contained gas and felt like a bladder filled half with gas and half with liquid gurgled loudly when pressed and on incision of the right ventricle gas escaped with a puff The brain was deeply engorged and there were many air emboli In this case death was due to a general escape of nitrogen within the blood stream

Treatment

Prophylactic Treatment—Since the malady is due entirely to nitrogen saturation of the tissues and the subsequent escape from solution of this gas into the tissues during a too rapid return to normal pressures it follows that the malady can always be prevented by adopting suitable period lengths for compression In the first place the malady never arises from compressions below plus 18 lbs to the square inch or roughly 40 feet of water and those who work at such a pressure may work long hours and return to a normal pressure rapidly and without any risk At higher pressures the

working shifts must be shortened as the pressure gets higher The shifts should be not longer than 6 to 8 hours at a pressure of 30 to 35 lbs or 3 atmospheres 2 to 3 hours at a pressure of 45 lbs and one hour only at a pressure of 50 lbs At higher pressures than this which are only encountered by divers a few minutes exposure is allowed only

Compressed air sickness never occurs if the return to the normal atmospheric pressure be sufficiently slow Animals can be exposed to very high pressures short of those causing oxygen poisoning with impunity provided they be decompressed slowly enough This decompression is carried out in the case of the diver by raising him to various levels in stages and letting him remain at each stage a longer and a longer period as the surface is approached In the case of caisson workers a series of air locked chambers is provided in which the air pressure is lowered in stages the men remaining longer and longer at each stage as they approach the normal pressure The important fact in connection with decompression is that the absolute pressure can always be halved forthwith without any risk In the first air lock on leaving the working face of a caisson for example the pressure is at once reduced to one half that of the working face and in the remaining air locks the pressure is reduced by stages until zero is reached

Leonard Hill has shown experimentally that it is always safe to lower the pressure to plus 20 lbs by gradual decompression during the space of ten minutes then to wait at that pressure for two hours and then bring the pressure to zero by gradual reduction in ten minutes The Admiralty rules for divers require that a diver working say at 140 feet shall be first raised straight away to a depth of 50 feet where he waits ten minutes then to 40 feet for ten minutes 30 feet for twenty minutes 20 feet for thirty minutes 10 feet for thirty five minutes and then he leaves the water abruptly The difficulty and danger is the tendency on the part of the workers to curtail these weary waits and get away from work as soon as possible It is important that all fat subjects and all those who have shown a susceptibility to compressed air sickness and all those not in absolutely sound bodily health shall be excluded from working in highly compressed air

Curative Treatment—It was early discovered by the caisson workers themselves that the only remedy for the malady was to re-enter the high air pressure A recompressing apparatus in the form of a medical air lock is now supplied at all caisson works and on all ships engaged in deep salvage On the appearance of any symptoms the worker is placed in the compressing room and the pressure is run up to the full pressure at which he has been working when it is usual for the symptoms to rapidly ameliorate or disappear After the recompression the decompression must be carried out very slowly for the bubbles once formed in the tissues are not easy to get rid of though they may be kept at a small size by the pressure

Cases apparently at the point of death with cyanosis and coma have *many times been completely recovered in a few hours by recompression* When symptoms have appeared the decompression should take at least five hours Caisson workers and divers should sleep and live close to the medical air lock so that they may be near aid during the first hours following decompression The paralysis when once established is to be treated upon ordinary lines

CHAPTER XVI

TUMORS OF THE SPINAL CORD AND OTHER LESIONS CAUSING COMPRESSION

By W. RUSSELL BRAIN

TABLE OF CONTENTS

Under this heading are united various morbid processes which narrow the lumen of the spinal canal and derange the functions of the spinal cord directly by injury of nervous structures or indirectly by interfering with their nutrition

GENERAL CONSIDERATIONS

The commonest causes of compression are tuberculosis especially spinal caries vertebral tumors which may be primary or secondary from growth elsewhere or due to direct spread from a growth in adjoining parts spinal tumors including cysts and injury Rarer causes are aneurysm syphilis and other acute and chronic inflammations

Signs and Symptoms

The effects of compression of the spinal cord vary with the nature and position of the disease Nevertheless the signs and symptoms in all cases have much in common and it is convenient first to consider them in a general description

Their characteristic feature is the combination of two sets of phenomena root symptoms at the level of the disease and cord symptoms below this point The first are evidenced by sensory signs of irritation or destruction of nerve roots and by motor signs of a lower neuron lesion the latter by signs of interruption of the conducting paths in the cord with the sensory signs of a transverse lesion and motor signs of an upper neuron lesion The presence of this combination is almost decisive for diagnosis and its importance cannot be overestimated

Root Symptoms —The chief of these is pain in the course of nerves or in parts supplied by the affected roots It is not common in spinal caries, but is the first symptom of compression in a very large majority of all other cases and may be the only symptom for months or even years It assumes various forms a dull ache a neuralgic pain a distressing feeling of constriction sharp cutting pains or a pain so excruciating as to render life unbearable It may be constant or intermittent, or a dull ache may be felt at intervals between severe paroxysms It is often greatly increased by movement of the spine As a rule the nerve trunks are not tender on pressure as in ordinary neuralgia The skin at first may be hypersensitive in the painful area but very soon its sensibility is diminished (anesthesia dolorosa) Severe paroxysmal pain may be felt along the course of nerves below the level of a lesion in the spinal cord This condition is commonest in intramedullary lesions and is worthy of special notice as it may be an early and puzzling symptom Pain in the legs with this cause has been diagnosed as sciatica and has been falsely appreciated as a root pain It may be helpful to remember that in most cases this pain of central origin" is more severe in the leg in which the loss of skin sensation is less a result which would not be expected if the pain were a true root symptom

Motor root symptoms are weakness loss of tone and wasting in the muscles supplied by the affected segment In many cases root symptom are absent throughout the course of the disease and the first effects of compression are referable to interruption of the conducting paths in the cord

Cord Symptoms —According to the tract first affected the first symptom may be motor or sensory In most cases it is motor but no mode of onset is constant Indeed this may vary in different cases where the lesions seem to be identical in nature and position

In a typical case with a slowly progressive lesion in the dorsal region a

feeling of stiffness or heaviness in one lower limb which comes on after walking is often the patient's earliest complaint At first it is only noticed after exertion and disappears with rest but by degrees the distance that can be covered without distress diminishes both legs are affected and at length perhaps only after months or even years of increasing difficulty walking becomes impossible

As the power in the legs diminishes stiffness develops and gradually increases until at length a condition arises in which the paralysed limbs are held rigidly extended at all joints by a powerful involuntary spasm like contraction of the extensor muscles In these stiff limbs which respond imperfectly or not at all to the will of the patient there may occur from time to time movements over which he has no control While the limbs are still rigid in extension this involuntary movement described by the patient as a trembling of the limb resembles exactly that obtained when ankle clonus is elicited it is indeed a spontaneous clonus of the leg and thigh muscles In more severe cases a different kind of movement occurs in which the legs are drawn up from time to time by involuntary contractions of the flexor muscles flexor spasm At first the intermissions between the spasms are complete and the limbs regain their extended position but as time goes on the spasms become more frequent complete relaxation no longer occurs and the limbs are held constantly in an attitude of flexion

Occasionally alterations in subjective sensation precede the motor symptoms by a considerable interval These paraesthesiae usually consist in a feeling of numbness or tingling in one or both legs but patients often use bizarre expressions in their attempts to describe them It is like a cold wind blowing on the leg like water trickling down under the skin as if the bones were made of ice and so on

Troubles with micturition frequency sudden imperative call delay and lastly incontinence are usually late symptoms It is often noticed that spincter control is perfect so long as one leg alone is weak and that bladder trouble begins when both are affected

Although variations are common in most cases the cord symptoms arise in the following order first weakness and spasticity then impairment of sensation position and passive movement temperature pain and touch being affected in progression Defective sphincter control often precedes and sometimes follows sensory loss Ultimately the limbs become flaccid the knee and ankle jerks are lost and the muscles waste

Motor Signs—It must be stated at once that in all that follows a physiological nomenclature is used according to which for reasons to be given later the muscles of the leg which dorsiflex the foot and toes are classed as flexors while those which plantarflex the foot and toes are grouped with the extensors

The condition arising in parts below the lesion from interruption of the motor paths in the cord is characterized by loss or diminution of voluntary power alteration in the tone of the muscles and in the attitude of the limbs changes in the deep and superficial reflexes and by the occurrence of certain reflex phenomena

The loss of power varies from a diminution in the rate or range or strength of a movement at one joint of one limb to complete immobility of both and depends on the degree of involvement of the pyramidal tracts In the early stages the weakness may be present after exertion only It is often greater in one limb than in the other It is more marked in the flexors than in the corresponding extensors and it begins first in the distal segments of the limb

The tone of the extensor group of muscles is relatively increased at an early period and on flexing the limbs passively considerable resistance is encountered it may even be impossible to overcome the rigidity Once the limb is flexed however the muscles become more supple and it is then possible to move the limb comparatively freely In some cases the spasm returns as the limb is again extended and completes the movement of extension itself like the spring of a knifeblade when a knife is being opened clasp knife rigidity "

This increase of tone in the extensor group of muscles in the lower limbs is characteristic of interruption of the pyramidal tract in any part of its course It is found in all pure pyramidal lesions and is a constant result of interference with this tract in the early stages of compression The combination of weakness and spasticity with extended lower limbs which occurs in compression and in other diseases of the spinal cord constitutes one of the forms of paraplegia and is known as "paraplegia in extension "

In cases where the lesion is more extensive and where in addition to the pyramidal tracts certain extrapyramidal motor paths are injured the extensor muscles lose their tone for which they depend on connections with the brain stem through these same extrapyramidal paths while the flexor group of muscles retains its tone which depends on a reflex arc which is purely spinal As a result the limbs are drawn up by the unopposed action of the flexors This condition of weakness and spasticity with flexed limbs constitutes the form of paraplegia known as "paraplegia in flexion In the transitional stage from paraplegia in extension to paraplegia in flexion the flexed position is occasional with flexor spasms due to spasmodic accessions of tone in the flexor muscles Later the flexed position becomes constant, though it varies in degree owing to the pull of the flexors which retain their normal tone against the extensors which gradually lose it In the later stage when the limbs are permanently flexed the characteristic phasic activity of the flexor group is still shown by the occurrence from

time to time either spontaneously or more likely in response to slight stimuli of sudden spasmodic increases in the tone of the muscles with a further drawing up of the limbs For a long time the attitude of the limbs is due entirely to these changes in tone but in the end contracture and shortening in the muscles and alterations in and around the joints occur and the deformities become permanent

Closely connected with this increase of tone in the extensor muscles is the exaggeration of the deep reflexes the knee and ankle jerks They give early evidence of interference with the pyramidal tract and a careful comparison of the reflexes in the two limbs may disclose the first organic sign of compression If in the absence of other signs the reflexes seem to be increased on both sides but are equally brisk no useful evidence has been obtained for variations in health are wide But if a difference however slight is found then decisive evidence of organic disease has been elicited In more advanced cases the exaggeration is obvious and ankle and knee clonus are often present If the condition advances from paraplegia in extension to paraplegia in flexion the character of the deep reflexes changes It is often stated that the deep reflexes are lost in paraplegia in flexion but this is not altogether true The knee jerk and ankle jerk are diminished or lost because as we saw above the extensor muscles lose their tone in this condition but if looked for it will be found that the jerks are still brisk in the only group of muscles which retains its tone namely in the flexors and that the hamstring jerks persist

The changes in the superficial reflexes below the level of the lesion are equally constant The abdominal and cremasteric reflexes are altered quantitatively They are diminished or abolished whereas the plantar reflex undergoes an extremely interesting and important qualitative change to the extensor plantar response Babinski s phenomenon

A diminution in the abdominal reflexes forms an early delicate and unequivocal sign of pyramidal tract disease a sign whose importance is not yet fully recognized Here again it is often a matter of comparison In health the variations are great and a diminution which is equal on both sides may be physiological But if there is a difference between the two sides at corresponding points then the pyramidal tract is certainly affected on the side of diminution This difference may not appear at once but may be distinct after repeated alternate stimulation of corresponding points on opposite sides when the reflex may be found to tire first on the affected side

No satisfactory explanation of the loss of abdominal reflexes in disease of the pyramidal tract has yet been given It is noteworthy that these reflexes are not present in animals lower than primates and that they do not appear in man until some months after birth They are phylogenetically

and ontogenetically recent (Brouwer) and it may be that following a law with wide general applications 'last to come first to go' they are therefore lost early in disease

The extensor plantar reponse is another certain sign of pyramidal tract disease and when it is well marked neither its presence nor its meaning is in doubt It may be extremely difficult however to decide the nature of the response in the early stages just at the time when this is of great importance for diagnosis Here again the importance of comparisons must be emphasized If from one sole a normal flexor response is obtained and on the other the nature of the response is doubtful the highest value may safely be given to this difference for it is almost as significant as if a definite extensor response had been elicited The pathological response appears earliest on stimulation of the outer part of the sole or outer border of the foot rarely it is obtained by pressing firmly from above downwards along the tibia and adjacent muscles (Oppenheim s sign) by compressing the calf muscles (Gordon s sign) or by pinching the téndo achillis (Schafer s sign) before it appears on stimulation of the sole of the foot

In the light of recent investigations (Marie and Foix Walshe) on reflex phenomena in spastic paralysis the nature of this 'extensor plantar response becomes clear on considering the movements which can be produced at will by appropriate stimulation of the paralyzed limbs The experiments of Sherrington made us familiar with these reflexes in spinal and decerebrate animals It is now known that the principles he laid down apply to man when by an experiment of nature the reflex centers in the spinal cord are liberated from higher control The most important of these reflexes and the only one which needs mention here is the flexion reflex of the lower limb It is best obtained by applying a hurtful stimulus such as a pin prick to the outer border of the sole and when fully developed consists in flexion of the hip and knee dorsiflexion of the foot and an upward movement physiological flexion of the great toe When this reflex is well marked as in cases of paraplegia in flexion the contraction of all the muscles of the physiological flexor group is shown by a definite movement of the limb at all its joints If however the reflex is feeble either in paraplegia in extension where the reflex has to overcome the maintained hypertonus of the extensor muscles or when from any cause almost all reflex activity has disappeared the response is minimal and can be detected in a few muscles only It has been demonstrated clearly that this minimal response is a contraction of the hamstrings and an extension" of the great toe

The so called extensor plantar response never occurs as an isolated phenomenon it is always accompanied by a contraction of flexor muscles other than those which dorsiflex the hallux It is not to be looked upon as an inexplicable independent sign of injury of the pyramidal tract but must

be recognized as an integral part of a general reflex flexion movement which occurs constantly in favorable conditions on appropriate stimulation when the spinal cord is freed from the full controlling influence of higher centers This reflex movement is exactly the same as that seen in an involuntary flexor spasm Each spasm is indeed a typical flexion reflex in response to a slight cutaneous stimulus

The normal plantar response is also accompanied by a contraction of certain thigh muscles but it is obtained from the sole alone whereas the receptive field of the pathological reflex is much wider and although this reflex is first and most easily obtained from the sole it can often be produced by stimulating the skin on any part of the limb When this is understood the nature of Oppenheim's sign and of many other signs which have been described as if they were isolated phenomena at once becomes clear The procedure in each is different but the result is the same in all—a flexion reflex of the lower limb whose most obvious component is an upward movement of the great toe

Sensory Signs —Sensory disturbances may arise like the motor in two ways from injury to nerve roots at the level of the lesion or by interference with the conducting paths in the cord Either set of structures may be earliest affected consequently the signs may appear first in the area of distribution of the roots arising from the affected segment or in parts below this level In a typical case of compression of the cord in the dorsal region motor signs are usually well marked before any sensory loss is found In some cases usually of spinal caries the paralysis of the limbs is complete while sensation is yet intact and it is a matter of general observation that no parallelism exists between the degree of motor and sensory disturbance The reverse condition great sensory loss with slight motor trouble is never seen in compression

It is here necessary to make a brief statement of the different forms of sensation and of their grouping and conduction in the spinal cord The forms of sensation which must be examined separately in each case fall into the following groups (a) touch superficial and deep (b) pain in the skin and in deeper structures (c) temperature and (d) sense of position and of passive movement together with the sense of vibration exact localization of touch and discrimination of two points When one or more of these groups is affected alone or out of proportion to the others sensation is said to be "dissociated It must be noted that the dissociations which arise in cord lesions differ entirely from those seen in lesions of peripheral nerves in other words that a complete regrouping of sensory fibers takes place in the spinal cord For example in peripheral nerve lesions pain is often dissociated superficial pain being lost while deep pain is retained or increased The sense of position and passive movement is lost with deep pain Light

and ontogenetically recent (Brouwer) and it may be that following a law with wide general applications last to come first to go' they are therefore lost early in disease

The extensor plantar reponse is another certain sign of pyramidal tract disease and when it is well marked neither its presence nor its meaning is in doubt It may be extremely difficult, however to decide the nature of the response in the early stages just at the time when this is of great importance for diagnosis Here again the importance of compari ons must be emphasized If from one sole a normal flexor response is obtained, and on the other the nature of the response is doubtful the highest value may safely be given to this difference for it is almost as significant as if a definite extensor response had been elicited The pathological response appears earliest on stimulation of the outer part of the sole or outer border of the foot rarely it is obtained by pressing firmly from above downwards along the tibia and adjacent muscles (Oppenheim s sign) by compressing the calf muscles (Gordon s sign) or by pinching the téndo achillis (Schafer s sign) before it appears on stimulation of the sole of the foot

In the light of recent investigations (Marie and Foix Walshe) on reflex phenomena in spastic paralysis the nature of this extensor plantar response becomes clear on considering the movements which can be produced at will by appropriate stimulation of the paralyzed limbs The experiments of Sherrington made us familiar with these reflexes in spinal and decerebrate animals It is now known that the principles he laid down apply to man when by an experiment of nature the reflex centers in the spinal cord are liberated from higher control The most important of these reflexes and the only one which needs mention here is the flexion reflex of the lower limb It is best obtained by applying a hurtful stimulus such as a pin prick to the outer border of the sole and when fully developed consists in flexion of the hip and knee dorsiflexion of the foot and an upward movement physiological flexion of the great toe When this reflex is well marked as in cases of paraplegia in flexion the contraction of all the muscles of the physiological flexor group is shown by a definite movement of the limb at all its joints If however the reflex is feeble either in paraplegia in extension where the reflex has to overcome the maintained hypertonus of the extensor muscles or when from any cause almost all reflex activity has disappeared the response is minimal and can be detected in a few muscles only It has been demonstrated clearly that this minimal response is a contraction of the hamstrings and an extension of the great toe

The so called extensor plantar response never occurs as an isolated phenomenon it is always accompanied by a contraction of flexor muscles other than those which dorsiflex the hallux It is not to be looked upon a an inexplicable independent sign of injury of the pyramidal tract but must

power (2) loss of sense of position and passive movement of vibration sense and of discrimination of two points (3) transitory hyperesthesia to touch pain and temperature (4) a zone of anesthesia corresponding to the posterior roots at the level of the lesion situated immediately above 3 (5) a zone of hyperesthesia immediately above 4 (6) elevation of temperature and other signs of vasomotor paralysis in the paralyzed parts often in zone 5 (b) on the side opposite to the lesion (1) retention of voluntary power (2) anesthesia to touch temperature and pain with its upper limit some distance below the level of the lesion (3) sense of position etc intact (4) a band of hyperesthesia above the anesthetic area

In compression this syndrome is often encountered in a modified form whilst in any case of paraplegia where the superficial sensory loss is greater in the leg in which most power is retained the expression modified Brown Séquard syndrome is used to describe the clinical findings In such cases the order in which sensation is lost on the side opposite to the lesion is usually first temperature then pain and lastly touch while loss of position and passive movement and vibration on the same side in the weaker limb appears very early and is often the very first sensory sign In cases where both legs are equally affected the degree of loss of sensation in all forms may be equal from the beginning but in most cases temperature pain and touch are impaired in this order The loss occurs first in one of two positions In the larger number of cases the soles of the feet first become less sensitive then the legs are affected and later the thighs The skin is involved in the order of the length of the sensory neurons supplying it (Collier) In a smaller number of cases the loss is first manifest over the most caudal segmental areas and extends upwards in segmental progression Finally whatever the mode of onset sensation of all kinds is diminished or lost in all parts below the lesion with the upper part of the anesthetic area corresponding to the segments affected by the lesion and the anesthesia in parts below arising from interruption of sensory tracts One exception to the statement that sensation is lost in all parts below the lesion must be made for it is often observed that with severe sensory loss in other parts below the lesion sensation in the distribution of the lowest sacral segments has been retained As the longest neurons in the cord lie nearest the periphery such an escape of sacral fibers would suggest an affection of the more mesial fibers of the sensory path

Cerebrospinal Fluid

Examination of the cerebrospinal fluid may reveal the sign which in chronic cases is pathognomonic of compression namely the presence of

touch may be dissociated from pressure, and temperature may be dissociated into two groups sensibility to slight alterations in temperature and sensibility to extreme degrees of temperature In lesions of the cord such dissociations never occur If pain is affected at all, superficial and deep pain are lost together The sense of position and passive movement forms a group quite distinct from deep pain Light touch and pressure are lost together Temperature is affected for all degrees alike and heat and cold may be lost independently As regards conduction in the cord the essential facts are that most of the touch fibers and all of those conveying pain and temperature after ascending for several segments in the gray matter finally cross by way of the anterior commissure to the anterolateral column of the opposite side whilst some touch fibers and those conveying sense of position and passive movement exact localization of touch vibration and discrimination of two points ascend in the posterior columns of the side on which they enter

The fibers which cross do not pass at once to the opposite side but take a diagonal course which varies in obliquity at different levels and for the different forms of sensation There is no crossing of fibers below the second lumbar segment In the middorsal region pain and temperature cross quickly and the decussation is complete one segment above the point of entry of the posterior roots which convey them to the cord while touch crosses more slowly and is complete in two segments The crossing becomes more oblique as the cord is ascended and in the upper dorsal region pain and temperature have crossed in two segments and touch in three while in the cervical enlargement the first cross in four segments the latter in five In the upper cervical region pain and temperature fibers ascend for five or six segments before all of them reach the opposite side

Knowledge in these matters is still incomplete but it can be stated confidently that pain crosses quickest then cold then heat and touch slowest of all Herein lies the explanation of two facts first that in unilateral lesions the upper limit of anesthesia on the opposite side due to injury of sensory paths in the cord is below the segmental level of the injury and secondly that the upper level is higher for one form of sensation than another The level is highest for that form which decussates most rapidly because fibers which cross slowly evade the lesion by ascending beyond it on the uninjured side before they cross, while those which cross quickly encounter it after crossing

In early cases of compression one side of the cord is often more affected than the other and the resulting combination of symptoms is known as *Brown Sequard's syndrome* For its production a complete accurate hemisection of the cord such as is sometimes caused by stab wounds is necessary Its features are (a) on the side of the lesion (1) loss of voluntary

changes visible radiographically save in rare cases in which a tumor erodes through the vertebral canal (so called dumb bell tumors)

Any source of spinal compression however usually can be demonstrated radiographically following the injection of lipiodol which is an oil opaque to x rays This is injected usually by cisternal puncture through the posterior occipito-atlantal ligament a lumbar puncture needle being introduced above the spinous process of the second cervical vertebra in the middle line in the plane of the external auditory meati and the nasion with the patient in the sitting posture One to two c c of lipiodol are injected when the point of the needle has reached the subarachnoid space and the downward passage of the oil within the spinal subarachnoid space is followed on the x ray screen Obstruction of the spinal subarachnoid space causes temporary or permanent arrest of the lipiodol at its upper level and this is recorded by taking x ray films Normally the lipiodol falls in one or two minutes to the level of the second sacral vertebra Tumors at the level of the foramen magnum are best demonstrated by injecting lipiodol by lumbar puncture and inverting the patient on a special x ray table

Pathology of Compression

In early cases or when the compression is slight the naked eye appearance of the cord often is normal Microscopically the only visible change is a swelling of the myelin sheaths and axis cylinders Later the myelin breaks down the nerve fibers degenerate spaces appear in the neuroglia the pericellular and perivascular lymphatics are dilated and often contain granular and fatty debris and numerous compound granular corpuscles

In severe or long standing cases the cord is flattened indented or uniformly diminished in size its consistence is increased on section it is grayish and the normal outlines between the white and gray matter are lost Microscopically there is an increase of interstitial tissue and widespread necrosis of the nervous elements In some cases the necrotic area are triangular with the base at the periphery of the cord and are due to thrombosis of degenerated intraspinal arteries The changes are most marked at the point of greatest compression In caries they are usually coterminous with the pachymeningitis but in many cases whatever the cause the changes extend over several segments above and below the affected point or isolated areas of necrosis may be found at some distance from it with normal tissue intervening

When attempts are made to correlate the pathological findings with the

the loculation syndrome In its complete form this consists in a great increase in the amount of albumin with absence or trivial increase in the number of cells and a yellow color in the fluid (xanthochromia) The normal amount of albumin is about 0 025 per cent In compression it is often increased a hundredfold or more readings above 1 per cent are very common 4 6 per cent has been recorded Sometimes the fluid clots in the test tube on cooling In the absence of evidence of syphilis 0 1 per cent of albumin with a low cell count is strong evidence of compression and as the amount of albumin increases the diagnosis becomes more certain Xanthochromia is common but its value as a sign of compression is slight as it is often absent when albumin is greatly increased and it is found in many other conditions such as intracranial tumors tuberculous meningitis acute poliomyelitis syphilitic spinal meningitis cerebrospinal meningitis and after cerebral and meningeal hemorrhages

These changes are found in the fluid below the site of compression only wherever this may be They are thought to be due to exudation of serum or small hemorrhages probably chiefly from the source of compression to a less extent from congested vessels of the spinal cord

Queckenstedt s Test — A most valuable sign of spinal compression is afforded by Queckenstedt s test With the patient lying on one side a manometer is attached to the lumbar puncture needle The resting pressure of the cerebrospinal fluid is observed and the jugular veins are then compressed Normally since the fluid in the lumbar sac is freely continuous with that in the cerebral subarachnoid space the rise of pressure produced in the latter by jugular compression is immediately conducted to the spinal manometer in which the fluid rapidly rises from the normal level of 120 mm of fluid to 300 mm of fluid or higher When the pressure on the jugulars is released the pressure in the manometer falls somewhat less rapidly If the spinal subarachnoid space is obstructed completely no rise of pressure occurs in the manometer on jugular compression though a slight rise may occur on compression of the abdomen Partial obstruction causes a slow and incomplete rise of pressure and a slower and more gradual fall

Radiography

Destructive lesions of the vertebral column such as primary and secondary neoplasms and tuberculous caries are visible on x ray examination which should be carried out in every case of suspected spinal compression Tumors arising within the vertebral canal produce no

changes visible radiographically save in rare cases in which a tumor erodes through the vertebral canal (so called dumb bell tumors)

Any source of spinal compression however usually can be demonstrated radiographically following the injection of lipiodol which is an oil opaque to x rays This is injected usually by cisternal puncture through the posterior occipito-atlantal ligament a lumbar puncture needle being introduced above the spinous process of the second cervical vertebra in the middle line in the plane of the external auditory meati and the nasion with the patient in the sitting posture One to two c c of lipiodol are injected when the point of the needle has reached the subarachnoid space and the downward passage of the oil within the spinal subarachnoid space is followed on the x ray screen Obstruction of the spinal subarachnoid space causes temporary or permanent arrest of the lipiodol at its upper level and this is recorded by taking x ray films Normally the lipiodol falls in one or two minutes to the level of the second sacral vertebra Tumors at the level of the foramen magnum are best demonstrated by injecting lipiodol by lumbar puncture and inverting the patient on a special x ray table

Pathology of Compression

In early cases or when the compression is slight the naked eye appearance of the cord often is normal Microscopically the only visible change is a swelling of the myelin sheaths and axis cylinders Later the myelin breaks down the nerve fibers degenerate spaces appear in the neuroglia the pericellular and perivascular lymphatics are dilated and often contain granular and fatty debris and numerous compound granular corpuscles

In severe or long standing cases the cord is flattened indented or uniformly diminished in size its consistence is increased on section it is grayish and the normal outlines between the white and gray matter are lost Microscopically there is an increase of interstitial tissue and wide spread necrosis of the nervous elements In some cases the necrotic areas are triangular with the base at the periphery of the cord and are due to thrombosis of degenerated intraspinal arteries The changes are most marked at the point of greatest compression In caries they are usually coterminous with the pachymeningitis but in many cases whatever the cause the changes extend over several segments above and below the affected point or isolated areas of necrosis may be found at some distance from it with normal tissue intervening

When attempts are made to correlate the pathological findings with th

symptoms it becomes evident that the one bears no constant relation to the other In one case of spinal caries for instance where a complete paraplegia was present the cord appears to be almost normal after death In another the cord as seen at operation appears to be hopelessly compressed by a tumor nevertheless considerable recovery of function takes place often with surprising rapidity, after the tumor is removed It is clear then on the one hand that some other factor than simple mechanical pressure must be active and on the other that the cord may be compressed for long periods with complete functional derangement but without any destruction of nervous tissues So long as pathologists attributed the symptoms to mechanical pressure or to compression myelitis it was impossible to explain these discrepancies In the light of modern conceptions of the pathology of compression however their mechanism is clear Stated briefly it may be said that the various morbid processes which narrow the lumen of the spinal canal produce their main effects on the cord by pressure on the veins and lymphatics in the epidural space in the dura mater and on the surface of the cord A simple localized edema is produced with swelling and softening of the nervous structures This edema may persist for long periods without causing anything more serious than a functional disturbance and when the cause of the edema is removed recovery takes place Such a mechanism accounts for fluctuations in the severity of the symptoms for cases with severe symptoms and slight pathological changes and for cases of rapid recovery after removal of the compressing agent

There remain cases in which the pathological changes are severe In these as a result of edema of long duration or of thrombosis of diseased vessels softening and necrosis occur and recovery of function is not to be expected These changes in the cord are not inflammatory but are identical with the softening seen in the brain as a result of vascular disturbance The name myelitis is not applicable to them and the use of the term compression myelitis should be discontinued

Spinal Tumors

New growths occur in the vertebral column (vertebral tumors) in the spinal membranes (meningeal tumors) and in the substance of the spinal cord (intramedullary tumors) In any of these situations the tumor may be primary or secondary from growth elsewhere or due to direct spread from a growth in adjoining parts Meningeal tumors are grouped as extradural and intradural the former outnumber the latter by two to one and of all meningeal tumors more than half are benign and removable

Vertebral Tumors

Sarcoma the commonest primary malignant tumor arises in the bone or periosteum of the bodies or laminæ often in several at once and may begin simultaneously at different levels of the spinal column Extension usually is rapid and the cord is compressed by the growth itself or by displaced bone or by a process of the growth which invades the spinal canal through an intervertebral foramen As a rule the dura mater sets bounds to its inward extension

Secondary sarcoma is not so common as the primary form It is frequently multiple and may arise by metastasis from sarcoma of bone elsewhere or by direct extension from a growth in adjoining soft parts e g from tumors in the mediastinal or retroperitoneal spaces In the latter type the dura mater may be surrounded by a noose of growth and a severe paraplegia due to acute edema of the cord is produced before the existence of the primary growth is suspected

Carcinoma of the vertebræ does not occur as a primary tumor but is a frequent and distressing complication of cancer elsewhere The bodies laminæ and intervertebral discs of several adjoining vertebræ are infiltrated so as to cause almost complete destruction of extensive portions of the spinal column

Several segments at different levels may be affected simultaneously almost every vertebra may be attacked Indeed it is sometimes possible after death to divide the spine with a knife from end to end The diseased areas collapse fractures dislocations and deformities are readily produced the cord is compressed and nerve roots are infiltrated by growth or nipped between displaced bone

A very small primary carcinoma in the breast thyroid or prostate for example may produce extensive disease of the vertebræ and disease of the bones is sometimes diagnosed before the site of the primary growth is discovered In fact this latter may be found only by careful examination after death

Rarer forms of malignant vertebral tumors are lymphosarcoma myeloma and melanotic sarcoma Benign tumors of the spine usually arise from the bodies of the vertebræ and grow forwards In rare instances however an osteoma an exostosis or a chondroma may encroach upon the lumen of the bony canal and compress the cord

Symptoms of Vertebral Tumors —The symptoms are of three kinds (1) those of the growth itself (2) those due to injury of nerve roots (3) those due to compression of the cord

Pain in the spine greatly increased by movement or pressure is almost

always present Deformity of the spine is common and may resemble that of caries but as several adjoining vertebræ often are equally affected the curve generally is less acute than in caries and when the growth is multiple more than one group of spines may be prominent and tender A palpable tumor is a rare symptom and usually a late one

The nerve root symptoms are of very great importance for they are often the first to appear, and for a long time they may be the only symptom They may cause great distress and their nature often is misunderstood The most prominent symptom is pain in the course of the affected roots Its special feature in vertebral tumors is the manner in which it is increased by movement

The cord symptoms are those of compression, and frequently the onset of paralysis is extremely rapid For example a patient complained of pain in the hip of two weeks duration This was found to be a root pain with partial anesthesia in the painful area but with no sign of compression of the cord A week later he walked to the hospital, apparently in the same condition but on the following day he developed retention of urine and within twenty four hours the lower limbs were completely paralyzed This mode of onset is commonest in cases of sarcoma in the mediastinal or retroperitoneal space where the growth directly infiltrates the vertebral bodies and surrounds the dura mater so rapidly that severe paralysis is the most prominent symptom when the patient is first seen

In these cases of rapid onset the limbs are flaccid sensory loss is great and there is retention of urine When the growth is primary in the vertebræ the onset of paralysis often is extremely slow it may take many months to become severe and then the limbs are spastic sensory loss may be slight or dissociated and frequency or incontinence of urine is the usual bladder symptom

The duration of the disease is measured by months in carcinoma or sarcoma spreading from adjoining parts and death is due to the malignant disease itself In slowly growing primary sarcoma of the vertebræ and in some cases of carcinoma life may be prolonged for years, and death is due rather to complications of the cord disease bedsores cystitis and kidney infection

Diagnosis of Vertebral Tumors —When root pains alone are present mistakes in diagnosis are common as the pain is often thought to be referred from the viscera or due to disease of parts in the course of the affected roots Thus angina pectoris gallstones renal colic hip disease sciatica and no doubt many other painful conditions have been diagnosed in early cases Once bone disease is detected the difficulty is to distinguish between caries and new growth Severe root pains and pain in the

spine both greatly increased by movement are strongly in favor of tumor as is *early sensory loss*

A history of carcinoma however remote even in the absence of signs of recurrence or the presence of malignant disease in other parts is overwhelming evidence against caries In the first half of life caries is more likely but later the two diseases are equally frequent In many cases the x ray evidence is decisive

Tumors Arising Within the Spinal Canal

These are considered together because although it is sometimes possible to distinguish between them the symptoms have much in common and in many cases a differential diagnosis is impossible

Vertebral tumors are nearly all malignant and the resulting nervous symptoms are in many cases merely complications of a disease already hopeless The group now to be considered is of greater interest for many of its forms are benign and all the symptoms are referable to an affection of nervous structures In this group tumors occur that provide for the neurologist and the surgeon a field in which combined knowledge and skill are applied with brilliant and life saving results

Tumors arising within the spinal canal are divided into extradural and intradural and the latter again into extramedullary and intramedullary according as they arise outside or within the spinal cord In Elsberg s series 19 per cent of spinal tumors were extradural 67 per cent were extramedullary and 14 per cent were intramedullary Thus extramedullary tumors the most favorable variety for surgical removal comprise two thirds of the total The commonest extramedullary tumors are endotheliomas and neurofibromas the former being about twice as common as the latter

Endotheliomas may arise either from the spinal nerve roots or from the meninges

The neurofibroma usually is a single rounded or almond shaped firm encapsuled non infiltrating tumor and is most often intradural In structure it is often transitional to neuroma myxoma or sarcoma It grows very slowly and two three even five or more years may elapse between the onset of the first symptom and the time when an accurate diagnosis with exact localization can be made

Other forms of extramedullary tumor are sarcoma which may be either localized or diffuse psammoma probably a calcified endothelioma myxoma lipoma angioma and chordoma The chordoma a rare malignant tumor arising from a remnant of the notochord usually is found in

always present Deformity of the spine is common and may resemble that of caries but as several adjoining vertebræ often are equally affected the curve generally is less acute than in caries and when the growth is multiple more than one group of spines may be prominent and tender A palpable tumor is a rare symptom and usually a late one

The nerve root symptoms are of very great importance for they are often the first to appear and for a long time they may be the only symptom They may cause great distress and their nature often is misunderstood The most prominent symptom is pain in the course of the affected roots Its special feature in vertebral tumors is the manner in which it is increased by movement

The cord symptoms are those of compression and frequently the onset of paralysis is extremely rapid For example a patient complained of pain in the hip of two weeks duration This was found to be a root pain with partial anesthesia in the painful area but with no sign of compression of the cord A week later he walked to the hospital apparently in the same condition but on the following day he developed retention of urine and within twenty four hours the lower limbs were completely paralyzed This mode of onset is commonest in cases of sarcoma in the mediastinal or retroperitoneal space where the growth directly infiltrates the vertebral bodies and surrounds the dura mater so rapidly that severe paralysis is the most prominent symptom when the patient is first seen

In these cases of rapid onset the limbs are flaccid sensory loss is great and there is retention of urine When the growth is primary in the vertebræ the onset of paralysis often is extremely slow it may take many months to become severe and then the limbs are spastic sensory loss may be slight or dissociated and frequency or incontinence of urine is the usual bladder symptom

The duration of the disease is measured by months in carcinoma or sarcoma spreading from adjoining parts and death is due to the malignant disease itself In slowly growing primary sarcoma of the vertebræ and in some cases of carcinoma life may be prolonged for years and death is due rather to complications of the cord disease bedsores cystitis and kidney infection

Diagnosis of Vertebral Tumors —When root pains alone are present mistakes in diagnosis are common as the pain is often thought to be referred from the viscera or due to disease of parts in the course of the affected roots Thus angina pectoris gallstones renal colic hip disease sciatica and no doubt many other painful conditions have been diagnosed in early cases Once bone disease is detected the difficulty is to distinguish between caries and new growth Severe root pains and pain in the

cord may be infiltrated cystic degeneration within the tumor is common and cavities indistinguishable from syringomyelia may be formed The growth does not extend beyond the medullary substance nor give rise to metastases

Primary solitary sarcoma of the spinal cord is very rare Infiltration with Hodgkin s lymphogranuloma and leukamic deposits are rare and usually are extradural Apart from solitary tubercles which are relatively common and gummata other forms of intramedullary tumors are extremely rare and need not be mentioned

Symptoms of Meningeal and Intramedullary Tumors — The characteristic symptoms of compression of the cord are nowhere better exemplified than in cases of slowly growing tumors of the meninges Pain of root distribution i present in the majority of cases It is usually very severe and may be the only symptom for months or even years At first it may be felt in one limb or on one side of the body alone later it is bilateral As a rule more than one root is affected and as the skin which may be hypersensitive at first soon loses its sensibility a band of anesthesia in the painful part is often the first physical sign

Motor root symptoms weakness and wasting of muscles and loss of deep reflexes are most easily observed in the limbs especially in the arms and in tumors at the level of the cervical enlargement they are often early and striking signs With tumors in the dorsal region wasting in the intercostal spaces or weakness in a segment of the muscles of the anterior abdominal wall is often readily observed

The cord symptoms usually appear late and progress slowly and as the tumor frequently begins at one side of the cord the paralysis in the lower limbs is often confined to one leg at first or is unequal and the Brown Sequard syndrome is common

The lower limbs when the growth is above the lumbar enlargement are usually rigid in extension Frequently the rigidity is moderate in degree Paraplegia in flexion is rare as most cases come to operation before this has developed

Sphincter disturbance usually is a late symptom It is often absent when one leg is weak but when both legs are weak there is usually some difficulty in bladder control Inability to hold the water when once the call is felt is the commonest trouble and in severe cases there is incontinence but it is surprising that in many cases with severe paralysis bladder symptoms are slight or absent

Increase of albumin with a low cell count in the cerebrospinal fluid is constant

Diagnosis of Meningeal and Intramedullary Tumors — A complete

the sacrococcygeal region Metastases from a cerebral glioma rarely spread to the spinal canal being carried by the cerebrospinal fluid and may produce the symptoms of a spinal tumor

Approximately two thirds of extramedullary tumors are situated in the posterior or postero lateral aspects of the cord and one third in the anterior or antero lateral aspect

Cysts parasitic and non parasitic may compress the spinal cord and produce symptoms indistinguishable from those of solid spinal tumors

Parasitic cysts in continental statistics account for about ten per cent of all spinal tumors but are not nearly so common in England Echino coccus cysts often invade the spinal canal from surrounding soft parts so that in many cases the tumor consists of a large extravertebral and a small intravertebral portion In rare instances they arise primarily from the dura or spread inwards from the vertebræ They are more often multiple than single and are nearly always extradural whereas cysticercus cysts which are much rarer are most often single and intradural

The etiology of non parasitic cysts is obscure They consist in collec tions of clear serous fluid circumscribed by slightly thickened adherent membranes A clear demonstration of the cyst is rare but its presence may sometimes be inferred at operation from the absence of the normal pulsations below it On puncturing the cyst which usually extends over several segments of the cord a small amount of fluid escapes under pres sure and the normal pulsations reappear More often however the cyst is opened during operation and the only evidence of its former presence is a flattening of the cord at the level at which a spinal tumor had been suspected before operation The name meningitis serosa circumscripta is applied to this condition

The dura mater forms an efficient barrier between the spinal cord and tumors of the vertebræ Carcinoma never penetrates it except in some cases at the level of the cauda equina sarcoma but rarely nor do menin geal tumors often invade the cord Most intramedullary growths there fore arise primarily within its substance

Intramedullary tumors corresponding histologically to most of the cerebral gliomas have been described Ependymomas constitute nearly one half of these and the remainder includes spongioblastomas astro blastomas medulloblastomas oligodendrogliomas ganglioneuromas and hemangioblastomas The gliomas usually are rapidly growing soft unen capsuled infiltrating tumors with ill defined limits At the seat of the growth the cord often appears to be uniformly enlarged In some cases the tumor is mainly unilateral the cord is deformed and the tumor may appear at the first glance to be extramedullary Long stretches of the

known the level of the tumor may be deduced by noting the highest point at which motor sensory or reflex disturbance is found

When the tumor is at the level of the cervical enlargement an exact localization usually is possible as evidence is gained on each point wasting of muscles is obvious sensory loss is easily detected whilst reflexe depending on different cervical segments can be readily compared Difficulty often arises in tumors of the dorsal region and here a careful examination is essential to ascertain the highest point at which sensation is impaired Each form of sensation must be tested for often one form is affected higher than another

If a large tuning fork is placed lightly on the skin and moved upwards over the anesthetic area the uppermost level of sensory loss is often obtained by noting the level at which the vibrations are first perceived On the thorax in order to eliminate bone conduction it is necessary to raise a fold of skin between the fingers before contact is made

Owing to the overlapping of the segmental sensory supply to the skin areas the line of demarcation is never abrupt but shades off gradually and it is often very difficult to make a segmental diagnosis on the sensory changes alone This enhances the value of motor localizing signs in lesions of the dorsal region and wasting or weakness of the muscles in an intercostal space is a sign of great value as these muscles have a unisegmental innervation Sometimes wasting is visible more often weakness is detected with the point of the finger when on inspiration instead of its being pressed outwards by the contracting muscles no contraction is felt or it sinks farther in

Loss of power in a segment of the rectus abdominis should be sought for carefully If the ninth dorsal segment is involved the rectus is paralyzed below a point one inch above the umbilicus and when the patient attempts to sit up the upper segment contracts and draws the umbilicus upwards excursion of the umbilicus If the lesion is at the eleventh dorsal segment the whole of the rectus contracts but the iliac regions bulge owing to paralysis of a part of the oblique muscles Another useful test is to note the highest point at which the abdominal reflex can be obtained above the lesion it is present at and below this level it is absent

Occasionally the tumor is found below the point indicated by the signs In these cases there is edema of the spinal cord in the segments above the tumor More often the tumor lies above the level predicted Of this the facts regarding the varying obliquity of the crossed sensory fibers at different levels provide an adequate explanation

The localization of tumors in the lumbosacral region presents special

diagnosis answers the questions (1) Is a tumor present? (2) Is it vertebral or intraspinal? (3) Is it meningeal or intramedullary? (4) What is the level of the tumor (segmental diagnosis)? Certain refinements of diagnosis may be attempted such as deciding the vertical extent of the tumor or its exact position within the cord or its pathological nature but it must be admitted that the very existence of a tumor is always in doubt until it is exposed that when found its position in relation to the membranes is often unexpected and that it is often several segments above sometimes below the point diagnosed

In the first place we must satisfy ourselves that the symptoms are due to compression If root and cord symptoms are both present the diagnosis up to this stage is rarely in doubt but if root pains and local signs in the spine are lacking it may be difficult and other focal diseases of the cord must be excluded Disseminated sclerosis is distinguished by remissions in the severity of the symptoms and by a history or signs of cranial nerve troubles syringomyelia by its slow course the nature of the sensory loss and trophic disturbances syphilis by examination of the blood and cerebrospinal fluid The demonstration of obstruction of the spinal subarachnoid space by Queckenstedt's test and the presence of the loculation syndrome are conclusive evidence of compression and this may be confirmed by radiography after the intrathecal injection of lipiodol

The next step after excluding caries is to decide whether the tumor is in the vertebræ or within the spinal canal Even at this state the difficulties may be great but local signs in the spine x ray findings the rapid course of the disease the very great increase of pain on movement or the discovery of new growth elsewhere may indicate vertebral tumor

The chief difference between the symptoms of intramedullary and extramedullary tumors is that in the latter root pains are present in the majority of cases and that they are usually severe and for a long time they alone may be present whereas in the former root pains usually are absent or slight In intramedullary lesions the symptoms often are bilateral from the beginning and the sensory loss may show the most profound dissociation e g almost complete loss to pain and temperature with unimpaired tactile sense

For practical purposes the exact segmental localization of the tumor is of much greater importance than its localization in depth for if that is given to guide the surgeon this will be decided in the only certain way by seeing the tumor

Segmental Diagnosis — At the point where the cord or its roots are compressed the functions of the affected segments motor sensory and reflex are impaired and as the function of each segment of the cord is

pend to a certain extent on the duration of the paralysis If the paralysis has lasted more than a year complete recovery of motor power is unusual although improvement usually is great on the other hand complete recovery has occurred after three years weakness in the legs (Sargent)

After operation recovery of power often is surprisingly rapid and may be noticeable in a few days In severe cases recovery of function occurs in the opposite order to its loss The knee jerks return there is a change from the flaccid to the spastic state and sensibility to touch pain and temperature return in progression Flexion of the toes is always the first movement to return The first sign of recovery may be that the patient is conscious of the passage of the excreta or of distention of the bladder

The extensor response and the loss of abdominal reflexes persist for months after the patient has regained full use of his limbs and the old level of sensory loss may still be detected years later

Intramedullary tumors usually are diffuse and irremovable but even in these cases temporary improvement may follow evacuation of a cystic tumor and in cases with root pain or pain below the lesion relief may be given by cutting the posterior roots or even by dividing the pain fibers in the anterolateral columns Operation is indicated in some cases of slowly growing vertebral sarcoma to relieve pressure or to prevent pain by cutting posterior roots

Tuberculosis of the Vertebræ

Tuberculosis of the vertebræ or spinal caries affects the cord in about one case in twenty and is the most frequent cause of compression paraplegia It is commonest in children and young adults but no age is exempt for the disease may begin in the sixth decade Compression arises most often from disease of the thoracic vertebræ Nervous symptoms arise in various ways and much has been written on the mechanism of their production

In most instances the disease extends to the loose tissue between the dura mater and the affected vertebral bodies the dura is infected (pachymeningitis externa) and the epidural space is filled with granulation tissue pus and caseous material This material may be present in sufficient quantity to compress the cord by its own bulk but it produces its effects mainly by obliterating the blood and lymph vessels in the dura and in the epidural space so interfering with the nutrition of the cord As a rule the inner surface of the dura is unaffected but in some cases adhesions form between it and the pia arachnoid In rare cases the inner surface of the

difficulties because owing to their long intraspinal course the nerve roots may be compressed far below the point at which they leave the cord so that the upper limit of sensory loss does not necessarily indicate the point of compression of the cord For example a tumor at the level of the second lumbar vertebra may injure all the roots of the cauda equina including the first lumbar root and cause anesthesia as high as the fold of the groin The upper level would be the same with a tumor compressing the first lumbar segment itself which is much higher, namely opposite the eleventh dorsal vertebra The clue is given by the difference in the motor and reflex signs with a lesion at the first lumbar segment the paralysis is due to an upper neuron lesion the limbs are weak but spastic and the knee and ankle jerks are exaggerated whereas if all the roots of the cauda equina are involved the paralysis is flaccid the muscles are wasted and the deep reflexes are absent The same reasoning applies to tumors at lower levels If for instance the lesion is at the level of the fourth lumbar segment the thigh muscles are wasted and the knee jerks are lost but the ankle jerks which depend on the integrity of the second sacral segment are retained In a cauda equina lesion affecting the fourth lumbar root the sacral roots are also constantly affected the motor defects in the limbs therefore are all those of a lower neuron lesion, so that the muscles below the knees are wasted also and the ankle jerks are lost

In conclusion if an operation is to be performed, we must know the relation of the affected segments to the spinous processes of the vertebræ This is obtained as follows in the cervical region to the number of the spine add one e g the fifth cervical spine lies over the sixth segment to the number of the first five dorsal spines add two e g the fifth dorsal spine corresponds to the seventh segment down to the tenth dorsal spine add three the tenth dorsal spine covers the first lumbar segment The eleventh dorsal spine corresponds to the third lumbar segment the twelfth to the first sacral The cord terminates just above the level of the first lumbar spine

Treatment of Spinal Tumors

If the symptoms point to an intraspinal tumor and a segmental diagnosis has been made immediate operation is indicated as it is the only treatment which can save the patient s life The operative mortality in skilled hands is low The outlook depends on the nature of the tumor for malignant growths recur but surprising temporary recoveries are made life is prolonged and pain is prevented by cutting sensory roots In the case of simple encapsuled tumors the prospects of complete recovery de

or to intramedullary parts of the lower motor neuron and this is most easily observed when the lesion is at the level of the cervical or lumbar enlargement

Herpes zoster in the course of the affected sensory roots is not very rare Its development sometimes gives a valuable clue to the diagnosis Disease affecting the eighth cervical or first dorsal roots usually causes paralysis of the sympathetic with narrowing of the palpebral fissure myosis enophthalmos and alterations in sweating on the face neck arm and upper part of the chest

Spinal Cord Symptoms — Cord symptoms frequently develop about a year after the curvature but variations are common and in some cases severe paralysis is present before the bone disease is detected On the other hand cord symptoms may develop in adults who have had a curvature since childhood Most often the onset is gradual and the paralysis takes several months to reach its maximum intensity Occasionally it is much more acute and in rare instances the paralysis may even be instantaneous or almost so in its appearance

Early signs are loss of power and increase in tone of the extensor muscles of the lower limbs increase in knee and ankle jerks diminution in the abdominal reflexes below the level of the lesion and the presence of an extensor plantar response As pressure on the cord increases the evolution of the phenomena already described as occurring in progressive spastic paraplegia may be observed

Sensory symptoms come later and usually are slight in degree compared with the loss of power As a rule all forms of sensation are equally affected dissociations are not uncommon but Brown Sequard s syndrome is extremely rare Sensory loss is a serious symptom for it betokens severe impairment of the vascular supply to the cord and when well marked it forms an indication for an early operation to relieve pressure When the paralysis is severe defective bladder control hasty or frequent micturition later urinary incontinence are common rectal control usually is retained until late in the progress of the disease

In disease of the upper cervical vertebræ pain is often referred to the occiput vomiting and slowing of the pulse may be produced by pressure on the medulla and nystagmus or sensory lo s on the face by pressure on the dorsal longitudinal bundle or on the spinal root of the fifth cranial nerve Further papilledema (optic neuritis) has been observed frequently in high cervical lesions (Collier and Taylor) The symptoms therefore may suggest an intracranial lesion but a good x ray picture and a careful examination of the posterior wall of the pharynx should prevent error in diagnosis

dura is infected secondary to disease of the bones while the outer surface is normal

The cord may also be compressed by a subperiosteal abscess on the dorsal surface of the vertebral bodies the dorsal portion of a diseased body may separate from the ventral part and move backwards against the cord a complete vertebral body may be so displaced sudden displacement and compression may be caused by trauma or the cord may be damaged by a loose spicule of bone

Of all the ways in which caries may lead to compression pachymeningitis is by far the commonest The other mechanisms it is said do not account for more than two per cent of the cases but some writers consider that this figure is too low

Tuberculosis of the cord and its membranes occurs in various forms quite apart from disease of the vertebræ, but these are not important for our present subject

Symptoms of Tuberculosis of the Vertebræ

The symptoms in caries may be due to (1) disease of the bone (2) affection of nerve roots (3) compression of the spinal cord

The chief bone symptoms are pain and tenderness in the spine at the affected part deformity and limitation of movement Pain is felt at first after walking or standing and disappears on lying down Later it is more constant It is increased by movement especially in the neck where the spine is more mobile Tenderness over the spines of the affected bodies is an early and most important sign It may be elicited by tapping the spine gently or firmer percussion even thumping may be necessary It is often felt when pressure is applied to the spines laterally or when an attempt is made to move them from side to side

Limitation of movement is obvious in the neck and in the dorsal and lumbar region it is often well seen when the patient picks up an object from the floor Deformity appears later than tenderness and it is most often sharply angular Sometimes however four or five bodies are diseased and the curvature is more rounded In some cases the displacement is lateral in others there is no deformity at all

Root Symptoms — In the majority of cases root symptoms are absent because the intervertebral foramina which lie close to the axis around which the bodies and spines rotate during their displacement are not narrowed and the roots escape damage Pain and anesthesia of root distribution are rare Weakness and wasting of muscles supplied by the segments at the level of the disease may be caused by damage to motor root

or to intramedullary parts of the lower motor neuron and this is most easily observed when the lesion is at the level of the cervical or lumbar enlargement

Herpes zoster in the course of the affected sensory roots is not very rare Its development sometimes gives a valuable clue to the diagnosis Disease affecting the eighth cervical or first dorsal roots usually causes paralysis of the sympathetic with narrowing of the palpebral fissure myosis enophthalmos and alterations in sweating on the face neck arm and upper part of the chest

Spinal Cord Symptoms — Cord symptoms frequently develop about a year after the curvature but variations are common and in some cases severe paralysis is present before the bone disease is detected On the other hand cord symptoms may develop in adults who have had a curvature since childhood Most often the onset is gradual and the paralysis takes several months to reach its maximum intensity Occasionally it is much more acute and in rare instances the paralysis may even be instantaneous or almost so in its appearance

Early signs are loss of power and increase in tone of the extensor muscles of the lower limbs increase in knee and ankle jerks diminution in the abdominal reflexes below the level of the lesion and the presence of an extensor plantar response As pressure on the cord increases the evolution of the phenomena already described as occurring in progressive spastic paraplegia may be observed

Sensory symptoms come later and usually are slight in degree compared with the loss of power As a rule all forms of sensation are equally affected dissociations are not uncommon but Brown Sequard s syndrome is extremely rare Sensory loss is a serious symptom for it betokens severe impairment of the vascular supply to the cord and when well marked it forms an indication for an early operation to relieve pressure When the paralysis is severe defective bladder control hasty or frequent micturition later urinary incontinence are common rectal control usually is retained until late in the progress of the disease

In disease of the upper cervical vertebræ pain is often referred to the occiput vomiting and slowing of the pulse may be produced by pressure on the medulla and nystagmus or sensory loss on the face by pressure on the dorsal longitudinal bundle or on the spinal root of the fifth cranial nerve Further papilledema (optic neuritis) has been observed frequently in high cervical lesions (Collier and Taylor) The symptoms therefore may suggest an intracranial lesion but a good x ray picture and a careful examination of the posterior wall of the pharynx should prevent error in diagnosis

dura is infected secondary to disease of the bones while the outer surface is normal

The cord may also be compressed by a subperiosteal abscess on the dorsal surface of the vertebral bodies the dorsal portion of a diseased body may separate from the ventral part and move backwards against the cord a complete vertebral body may be so displaced sudden displacement and compression may be caused by trauma, or the cord may be damaged by a loose spicule of bone

Of all the ways in which caries may lead to compression pachymeningitis is by far the commonest The other mechanisms it is said do not account for more than two per cent of the cases but some writers consider that this figure is too low

Tuberculosis of the cord and its membranes occurs in various forms quite apart from disease of the vertebræ but these are not important for our present subject

Symptoms of Tuberculosis of the Vertebræ

The symptoms in caries may be due to (1) disease of the bone (2) affection of nerve roots (3) compression of the spinal cord

The chief bone symptoms are pain and tenderness in the spine at the affected part deformity and limitation of movement Pain is felt at first after walking or standing and disappears on lying down Later it is more constant It is increased by movement, especially in the neck where the spine is more mobile Tenderness over the spines of the affected bodies is an early and most important sign It may be elicited by tapping the spine gently or firmer percussion even thumping may be necessary It is often felt when pressure is applied to the spines laterally or when an attempt is made to move them from side to side

Limitation of movement is obvious in the neck and in the dorsal and lumbar region it is often well seen when the patient picks up an object from the floor Deformity appears later than tenderness and it is most often sharply angular Sometimes however four or five bodies are diseased and the curvature is more rounded In some cases the displacement is lateral, in others there is no deformity at all

Root Symptoms — In the majority of cases root symptoms are absent because the intervertebral foramina which lie close to the axis around which the bodies and spines rotate during their displacement are not narrowed and the roots escape damage Pain and anesthesia of root distribution are rare Weakness and wasting of muscles supplied by the segments at the level of the disease may be caused by damage to motor roots

seminated sclerosis In hysteria and neurasthenia pains and tenderness in the spine are common symptoms but they are more diffuse and are not referred constantly to one place always and alone In chronic cases a high albumin and low cell content in the cerebrospinal fluid exclude at once all conditions other than compression

Treatment of Tuberculosis of the Vertebræ

The aim of treatment is to cure the bone disease for if this is obtained improvement in the nervous symptoms usually follows Complete rest on the back for many months is the routine treatment at present At the same time efforts are made to improve the general condition of the patient by providing fresh air and good food in plenty

When the disease is actively progressing treatment consists of hyper extension of the spine and subsequent fixation This may be obtained by means of a Bradford frame or a plaster bed to be followed by a plas ter jacket when the patient is well enough for ambulatory treatment In favorable cases improvement in the signs of spinal compression may be expected to begin within a month or two of immobilisation but rest on the back must be continued until the patient s general condition local signs and x ray appearances indicate that healing has occurred which may take one or even two years

When there is reason to think that the spinal compression is due to a retromediastinal abscess rapid relief may follow the operation of costo transversectomy Allbee s operation in which a bone graft from the tibia is inserted into the spinous processes above and below the affected ver tebræ is a surgical method of obtaining support and immobilisation of the spine It is mainly applicable to adults and has the advantage of shortening the period of rest in bed very considerably

Laminectomy is rarely indicated since bony pressure seldom plays any part in producing the spinal symptoms in Pott s disease Even when there is a very acute angular deformity removal of the laminal arches does nothing to relieve the tension exerted on the spinal cord anteriorly and may cause further vertebral collapse This operation should only be performed when there is reason to suspect that the spinal compression is due to bony pressure especially when this has occurred suddenly or when paralysis remains after the bone disease is cured and when the nervous symptoms suggest that the damage to the cord is not irremediable

In those cases in which spinal compression develops many years after the onset of the spinal caries treatment is almost always conserva tive

Course and Prognosis

The course of the bone disease does not necessarily run parallel with the nervous trouble Either may alter in severity independently, and frequently the caries is cured, but severe paralysis remains Many young people make a perfect recovery but in the majority of all cases recovery though considerable is incomplete Such recovery, as does occur, usually is permanent and relapses are surprisingly rare The outlook is best in children and when the disease is in the dorsal region So long as the limbs remain in the extended position recovery may be confidently expected but if paraplegia in flexion develops the outlook is not so good Nevertheless cases with signs of complete physiological division of the spinal cord have been known to recover In fatal cases death usually is due to sepsis from bedsores ascending infection of the urinary tract chest complications or tuberculous disease elsewhere

Diagnosis of Tuberculosis of the Vertebræ

When signs of compression develop in a patient who is known to be suffering from caries the cause is obvious Difficulty arises when the bone and cord symptoms come on together or when the nervous symptoms appear first Caries must be suspected in every case of spastic paraplegia for of this it is a common cause and in general no other diagnosis is justifiable until it has been excluded This implies careful and repeated examinations of the spine Even in the absence of deformity tenderness which is always found in the same place is of great significance and if the nervous symptoms are those which would be expected from disease of the segments underlying the tender spot then disease of the bones is almost certain In young people disease of the bone means caries in the great majority of cases In adults caries is still the most likely condition but vertebral new growths and aneurysm must be considered Absence of root symptoms though common in caries is unlikely in vertebral new growth An aneurysm would show other signs Moreover the x ray evidence usually enables us to distinguish between these three conditions

Syphilis is excluded by the routine examination of the blood and cerebrospinal fluid which should be made in every case of nervous disease Amyotrophic lateral sclerosis may be suggested by wasting in the hands and signs of pyramidal disease in the lower limbs but sensory loss or bone symptoms would decide against it A careful history with special reference to transient diplopia and bladder troubles and to remissions in the severity of the paralysis and signs of cranial nerve trouble should distinguish dis

CHAPTER XXII

TRAUMATIC AFFECTIONS OF THE SPINAL CORD

By N. S. ALCOCK

Table of Contents

Introduction

The spinal cord lies entirely within the bony surround of the vertebral canal. Injury to it therefore is in general consequent on injury to the structures which make up the vertebral column. Injury to the spinal cord is, however, so much more important that if present it should unquestionably take precedence and the bony injury be regarded as of secondary significance. Usually the cord is damaged at the same time as the injury but in certain circumstances it may be involved in the later effects.

In the immediate cases apart from the obvious mechanisms fractures and dislocations of the vertebrae gun shot wounds and rare stab wounds the cord may be damaged by less evident means. Thus, in the cervical region it is possible for the vertebrae to be momentarily dislocated

SYPHILIS OF THE VERTEBRAE

Tertiary syphilis may produce changes in the spine not unlike those of tuberculosis with periostitis and osteitis of the vertebral bodies and laminæ abundant granulation tissue firm or caseous gummatous masses and even caries of the bones extensive enough to cause a definite kyphosis The condition is very rare the cervical region is most often affected and the spinal cord may be compressed Other forms of syphilis of the cord and its membranes are considered in another article

Aneurysm of the aorta is a well known but rare cause of spinal compression The dorsal region usually is affected three or four vertebræ being slowly eroded from the left side until the dura mater is exposed and the cord compressed Sudden rupture of the aneurysm into the spinal canal has been described

OTHER ACUTE AND CHRONIC INFLAMMATIONS

Under this heading it is sufficient to mention acute osteomyelitis and periostitis spondylitis deformans Paget s disease and spondylitis rheumatica as rare but possible causes of spinal compression

Sept 1 1937

when the level of the lesion is high scratching the sole of the foot may evoke a downward movement of the toes (Guillain and Barre Holmes) The skin is dry the lower extremities lose heat more rapidly than do those of the normal individual and they swell if allowed to hang down The resistance of the affected tissues to infection is so lowered that *slight abrasions soon become septic and rapidly develop into ulcerating* bed sores

Stage of Reflex Activity —The effects of shock begin to pass off in from one to three weeks but if septic complications supervene depression of reflex function may be prolonged till the patient dies Severe toxemia or septicemia developing at this stage of diminished physiological resistance either kills the patient early or leads to dystrophic changes in the cord so that the reflex arcs are damaged temporarily or permanently

'But in the absence of septic infection periodic flexor movements confined at first to the feet make their appearance and in response to nocuous stimulation (scratching) of the sole contraction of the hamstrings is found to accompany downward movement of the toes As reflex excitability increases the toe response changes and the complete flexion reflex of the lower limb is obtained This consists of flexion at hip and knee dorsiflexion of the foot and upgoing toes a reaction of which Babinski s extensor response is an integral part as Walshe (1914) has proved clearly The receptive field of this reflex at first confined to the sole of the foot gradually invades the whole lower limb including both superficial and deep tissues Concurrently with extension of the reflexogenous zone the reflex effect from stimulation becomes more widespread Flexion of the stimulated limb is accompanied by a response in the opposite limb which usually is flexor but sometimes extensor and by contraction of the muscles of the anterior abdominal wall Scratching the skin of the abdomen evokes retraction of its muscular wall and cremasteric bulbocavernosus and anal reflexes are excited by appropriate stimulation At this stage the unfortunate patient begins to be tormented periodically with flexor spasms of the lower limbs and trunk which may become so vigorous as almost to jerk him out of bed

Erection of the penis occurs spontaneously and can be excited readily by to and fro movements of the prepuce over the glans penis which may lead to emission of semen As a rule a week or more elapses after the appearance of the flexion reflex before knee and ankle jerks can be evoked but when they return they may be quite brisk The extensor muscles however remain hypotonic

sufficiently far to damage the cervical cord, even to the point of transection only to return to apparent normality before the patient is seen (Munro, 1943) Haemorrhage into the cord, haematomyelia, may occur in association with a fall or jolt without bony injury Concussion of the spinal cord may be caused by direct or indirect blows to the vertebral bodies even though they are themselves not obviously damaged or for instance when a shell fragment strikes the vertebral column but does not directly hit the spinal cord It has been suggested that the near passage of a missile or blast may cause spinal concussion but if so it must be very rare, and Jefferson (1943) was able to say, "so far in our country, where we have had more bombs than in many other places no example of blast injury of the nervous system has been observed"

Of the delayed effects the commonest are consequent on injuries to the intervertebral discs, allowing the nucleus to protrude and press either on the roots or on the cord It is generally agreed also that trauma plays a material part in producing the lesion known as meningitis circumscripta serosa or arachnoiditis, and at one time or another many other spinal diseases have been thought to be due to, or aggravated by, trauma but the evidence cannot be considered convincing

Clinical Picture

Complete Division of the Spinal Cord

Riddoch s description of the clinical picture after transection of the cord is still the classical work and is given here in his own words He describes it under three headings '(1) stage of muscular flaccidity or spinal shock (2) stage of reflex activity and (3) stage of gradual failure of reflex functions

'1 *Stage of Muscular Flaccidity* —When the injury to the spinal cord is sudden as from a high velocity bullet or fracture-dislocation of the vertebral column there is immediate and complete flaccid paralysis and loss of sensibility with almost entire suppression of reflex action below the level corresponding to the lesion There is retention of urine and feces due to tonic contraction of the sphincters and atony of the detrusors of the bladder and rectum Priapism, which often is present immediately after the injury and is the result of venous engorgement soon is replaced by flaccidity of the penis Abdominal cremasteric and usually the bulbocavernosus and anal reflexes are abolished Knee and ankle jerks cannot be obtained The plantar reflexes may be absent but

occurs the mass reflex is less easy to evoke and somatic and visceral activities gain a certain degree of independence

3 *Stage of Gradual Failure of Reflex Activity* —If the general health of the patient is maintained at a high standard the stage of reflex activity may go on indefinitely But in the presence of intercurrent disease for example septic infection of the urinary tract the reflex functions of the cord deteriorate With each acute febrile exacerbation the reflexes become more difficult to evoke those of the extensor system disappearing earliest The muscles waste and the skin requires constant attention The bladder becomes smaller and retention of urine may return before the patient dies

Incomplete Division of the Spinal Cord

'After any severe injury of the spinal cord the function of the distal segments may for a time be almost entirely suppressed so that it is impossible to determine at this period whether or not the lesion is subtotal In a few days this depression of function begins to pass off and voluntary power and sensibility may return or certain reflex reactions may emerge which indicate that the lesion is incomplete

An outstanding reflex phenomenon of incomplete lesions of the spinal cord is a tonic contraction of the extensor muscles of the trunk and lower extremities which is called spasticity This pattern of hypertonus which is observed also in the lower limb in hemiplegia is in many ways similar to the decerebrate rigidity in animals which Sherrington described as reflex posture or standing It is a proprioceptive reflex reaction in antigravity muscles and the impulses which excite it originate in the receptors of the muscles themselves and their tendons and fascial sheaths When the patient tries to stand this extensor rigidity may be reinforced by another reflex mechanism the stutz reaktion or standing thrust which is excited by pressure on the sole of the foot In a case of spastic paraplegia if voluntary power is present the difficulty experienced by the patient in using it is not in extending his lower limbs or supporting his weight but in bending his limbs In spite of this extensor rigidity flexion reflexes are obtained readily by nocuous stimulation of the sole of the foot Evacuation of urine and other visceral reactions are not however excited in association with them and reflex micturition is not accompanied by flexor spasms

In occasional cases of subtotal transection of the spinal cord para

'Excessive sweating is often an outstanding manifestation of the sensitive condition of the reflex arcs to stimulation The area of skin, from which the sweat pours varies with the level of the spinal lesion but it does not coincide with the area of anesthesia The extent of the sudorific area is determined by the level at which the connector nerves which form the communication between the spinal cord and the sympathetic nervous system proper, are shut off from the influence of head ward centers Physiologically speaking, the sweating surface, like the area of anesthesia, lies below the level of the spinal lesion Thus, when the injury lies above the second thoracic segment of the cord the sudorific area may cover the whole surface of the body, with transection through the third or fourth thoracic segment hyperidrosis may be present on the lower extremities and trunk up to the clavicles and on the inner aspect of the upper limbs, and when the lesion is situated about the eighth or ninth thoracic segment, the area of sweating approximately corresponds with that of sensory loss But as soon as the spinal lesion lies below this point, hyperidrosis does not extend so high as the loss of sensibility

'The characteristic reaction of the flexed form of paralysis is the mass reflex In response to harmful stimuli such as a scratch or a prick applied to any paralysed part a vigorous bilateral flexor spasm of the lower limbs is evoked and if the level of the lesion be high enough the trunk is involved also in the movement Following the spasm the trunk and limbs resume their former posture, not from contraction of the extensors but from relaxation of the flexors and the pull of gravity It is a uniphasic stereotyped movement of violent nature in which the flexor muscles only are actively involved Moreover the energy liberated by the stimulus overflows into visceral channels The skin within the sudorific area becomes moist with sweat, and the bladder evacuates its contents, though in amount the urine may be less than half the quantity with which the bladder usually reacts Visceral as well as somatic stimuli excite the mass reflex Intestinal irritation inflammation of the urinary tract reflex expulsion of urine or feces are capable of evoking flexor spasms Visceral and somatic reactions mutually facilitate one another

The isolated spinal cord may never get beyond this stage of uncontrolled flexor activity Cases however are on record in which extension of the lower limbs could be obtained ultimately as a primary response and in which reflex flexion was followed by extension When this

occurs the mass reflex is less easy to evoke and somatic and visceral activities gain a certain degree of independence

3 *Stage of Gradual Failure of Reflex Activity* —If the general health of the patient is maintained at a high standard the stage of reflex activity may go on indefinitely But in the presence of intercurrent disease for example septic infection of the urinary tract the reflex functions of the cord deteriorate With each acute febrile exacerbation the reflexes become more difficult to evoke those of the extensor system disappearing earliest The muscles waste and the skin requires constant attention The bladder becomes smaller and retention of urine may return before the patient dies

Incomplete Division of the Spinal Cord

After any severe injury of the spinal cord the function of the distal segments may for a time be almost entirely suppressed so that it is impossible to determine at this period whether or not the lesion is sub total In a few days this depression of function begins to pass off and voluntary power and sensibility may return or certain reflex reactions may emerge which indicate that the lesion is incomplete

An outstanding reflex phenomenon of incomplete lesions of the spinal cord is a tonic contraction of the extensor muscles of the trunk and lower extremities which is called spasticity This pattern of hyper tonus which is observed also in the lower limb in hemiplegia is in many ways similar to the decerebrate rigidity in animals which Sherrington described as reflex posture or standing It is a proprioceptive reflex reaction in antigravity muscles and the impulses which excite it originate in the receptors of the muscles themselves and their tendons and fascial sheaths When the patient tries to stand this extensor rigidity may be reinforced by another reflex mechanism the stutz reaktion or standing thrust which is excited by pressure on the sole of the foot In a case of spastic paraplegia if voluntary power is present the difficulty experienced by the patient in using it is not in extending his lower limbs or supporting his weight but in bending his limbs In spite of this extensor rigidity flexion reflexes are obtained readily by nocuous stimulation of the sole of the foot Evacuation of urine and other visceral reactions are not however excited in association with them and reflex micturition is not accompanied by flexor spasms

In occasional cases of sub total transection of the spinal cord para

plegia in flexion is seen and is accompanied by severe flexor spasms with involuntary evacuation of urine and, at times, of feces

The residual condition after injuries to the thoracic portion of the cord is usually a spastic paraplegia of considerable degree In many cases the weakness and spasticity are much more pronounced in one lower limb than in the other, and in many there is a partial Brown Sequard syndrome, i e the motor impairment is much greater in one limb and the impairment of pain and temperature appreciation greater in the other The Brown-Sequard syndrome in its pure form is produced by a lesion of one lateral half of the spinal cord in the thoracic or cervical region and consists of spastic paralysis on the affected side below the level of the lesion due to interruption of the pyramidal (cortico spinal) tract, loss of sense of position on the same side owing to interruption of the ascending fibres in the posterior column, and loss of pain and temperature appreciation on the contralateral side as a result of interruption of the spinothalamic tract which is composed of ascending fibres which have crossed from the other side of the cord About the level of the lesion the sensory disturbance is likely to be complicated by the effects of injuries of some of the posterior (sensory) roots, and the local sensory picture is, therefore mixed

The degree to which vesical and rectal functions are disturbed with incomplete lesions of the cord varies with the severity of the spinal injury When this is slight, retention of urine and feces is quickly replaced by periodic reflex evacuation and this again by return of voluntary power But with gross injuries the period of retention lasts on an average for about three weeks before the reflex arcs emerge from the influence of spinal shock Sexual activity rarely recovers completely, and as a rule seminal emission is absent long after erections of the penis are evoked by psychical stimulation

Treatment

The advance of medicine between the two wars is well exemplified by the treatment of spinal cord injuries Riddoch's third stage must now be considered not as an inevitable sequel but as a failure of proper treatment and the aim should be to obtain a patient ambulant with splints with complete sphincter control and even able to earn his own living despite a complete transverse lesion of the cord

The recognition of the importance of sepsis is the keynote to treat

ment If sepsis is avoided then the above can be achieved from the very outset all measures are primarily directed to this end The two sources of sepsis are the bladder and the skin

First Aid Treatment

It is agreed that it is vitally important for correct treatment to start from the moment of injury and transportation of the patient from the scene of the accident to hospital must be carefully organized to prevent any further damage to the cord occurring The aim must be neither to flex rotate nor overextend his spine This is particularly true of cervical lesions where flexion may well cause sudden death There has been much discussion on the best way to ensure these points and the general consensus of opinion is that these patients should be moved on their back with the normal spinal curves maintained by pads such as a folded coat or the like Munro (1943) disagrees however and urges strongly that cervical lesions at least should be transported face downwards arguing that in this position there is less risk of neck flexion either by the patient trying to sit up or by helpful but inexperienced assistants

The Bladder

Correct handling of the bladder is of paramount importance from the very onset of treatment The avoidance of sepsis and the maintenance of the normal bladder size mean not only the chance of an ambulant dry life but in many cases determine the survival of the patient

After transections of the cord initially in the stage of spinal shock the bladder is atonic that is the detrusor muscle does not contract at all the internal sphincter remains closed and unresponsive to any stimulus the external sphincter relaxed and anal and bulbocavernosus reflexes absent In this state the bladder gradually fills and any emptying that occurs is only the result of leakage through the contracted internal sphincter and takes place because of the elasticity of the bladder wall and not by virtue of any contractile effort on its part

This stage is gradually succeeded by the autonomous bladder, so called because it is believed that the bladder is under neural control by the intramural autonomous plexus In this state the internal sphincter is hypertonic the detrusor contractions insufficient to overcome com

plegia in flexion is seen and is accompanied by severe flexor spasms with involuntary evacuation of urine and at times of feces

The residual condition after injuries to the thoracic portion of the cord is usually a spastic paraplegia of considerable degree In many cases the weakness and spasticity are much more pronounced in one lower limb than in the other, and in many there is a partial Brown Sequard syndrome, i e the motor impairment is much greater in one limb and the impairment of pain and temperature appreciation greater in the other The Brown Sequard syndrome in its pure form is produced by a lesion of one lateral half of the spinal cord in the thoracic or cervical region and consists of spastic paralysis on the affected side below the level of the lesion due to interruption of the pyramidal (cortico spinal) tract, loss of sense of position on the same side owing to interruption of the ascending fibres in the posterior column, and loss of pain and temperature appreciation on the contralateral side as a result of interruption of the spinothalamic tract which is composed of ascending fibres which have crossed from the other side of the cord About the level of the lesion the sensory disturbance is likely to be complicated by the effects of injuries of some of the posterior (sensory) roots, and the local sensory picture is, therefore, mixed

'The degree to which vesical and rectal functions are disturbed with incomplete lesions of the cord varies with the severity of the spinal injury When this is slight retention of urine and feces is quickly replaced by periodic reflex evacuation and this again by return of voluntary power But with gross injuries the period of retention lasts on an average for about three weeks before the reflex arcs emerge from the influence of spinal shock Sexual activity rarely recovers completely, and as a rule, seminal emission is absent long after erections of the penis are evoked by psychical stimulation"

Treatment

The advance of medicine between the two wars is well exemplified by the treatment of spinal cord injuries Riddoch's third stage must now be considered not as an inevitable sequel but as a failure of proper treatment and the aim should be to obtain a patient ambulant with splints with complete sphincter control and even able to earn his own living despite a complete transverse lesion of the cord

The recognition of the importance of sepsis is the keynote to treat

ment If sepsis is avoided then the above can be achieved from the very outset all measures are primarily directed to this end The two sources of sepsis are the bladder and the skin

First Aid Treatment

It is agreed that it is vitally important for correct treatment to start *from the moment of injury and transportation of the patient from the* scene of the accident to hospital must be carefully organized to prevent any further damage to the cord occurring The aim must be neither to flex rotate nor overextend his spine This is particularly true of cervical lesions where flexion may well cause sudden death There has been much discussion on the best way to ensure these points and the general consensus of opinion is that these patients should be moved on their back with the normal spinal curves maintained by pads such as a folded coat or the like Munro (1943) disagrees however and urges strongly that cervical lesions at least should be transported face downwards arguing that in this position there is less risk of neck flexion either by the patient trying to sit up or by helpful but inexperienced assistants

The Bladder

Correct *handling of the bladder is of paramount importance from* the very onset of treatment The avoidance of sepsis and the maintenance of the normal bladder size mean not only the chance of an ambulant dry life but in many cases determine the survival of the patient

After transections of the cord initially in the stage of spinal shock the bladder is atonic that is the detrusor muscle does not contract at all the internal sphincter remains closed and unresponsive to any stimulus the external sphincter relaxed and anal and bulbocavernosus reflexes absent In this state the bladder gradually fills and any emptying that occurs is only the result of leakage through the contracted internal sphincter and takes place because of the elasticity of the bladder wall and not by virtue of any contractile effort on its part

This stage is gradually succeeded by the autonomous bladder so called because it is believed that the bladder is under neural control by the intramural autonomous plexus In this state the internal sphincter is hypertonic the detrusor contractions insufficient to overcome com

pletely the sphincter tone, and emptying is inefficient but may be helped by voluntary muscles Some residual urine is always present While at first the bladder capacity is normal, it steadily tends to lessen as hyper trophy and contracture of the wall takes place until finally it may only hold 30 to 50 c c, and there is continual dribbling incontinence This is the final state in complete cauda lesions but where there is an actively reflex *lower portion of the cord, the bladder progresses to the reflex* bladder In this the detrusor contracts reflexly and completely in response to the sensory stimulus provided by the stretch of the critically filled bladder If the bladder capacity has been maintained, this type of bladder, although quite independent of any cerebral control, may be trained to empty at regular, not too frequent, intervals and with an intelligent patient there need be no incontinence either by day or night

This progression, however, is by no means inevitable It depends on the avoidance of any detrimental factor either local or general If at any stage the patient develops a urinary infection, or if there is septic absorption from sores toxaemia or hypo-proteinaemia, progress will cease If the condition is severe, the bladder control may even revert to a completely atonic state again

There is still, however, by no means complete agreement as to the best management for the neurogenic bladder In the initial stage of atonic retention, intermittent catheterisation or the ordinary indwelling catheter inevitably lead to severe sepsis and are to be condemned During the recent war the routine treatment has been a suprapubic cystotomy, but although this appears attractive as an early measure, the later effects may be deplorable It by no means ensures a freedom from infection it leads to a small contracted bladder and the eventual closure of the fistula may be very difficult Leaving the bladder alone to fill and over flow has at least the advantage of avoiding the introduction of sepsis and although this may result in overstretching the muscles and undesirable leaking of urine over anaesthetic areas it is generally held that this is safe for 36 hours if need be After this the method of choice lies between a small suprapubic catheter introduced through a leak proof junction high up on the abdominal wall combined with tidal drainage as recommended by Riches (1943) and urethral tidal drainage which Munro has advocated so consistently Either method requires care and supervision and the importance of keeping the urine sterile cannot be over emphasized Once the urine is infected it is much more difficult to control and once this has occurred there is always the possibility of stone formation to complicate the picture Two of the most useful

measures to avoid ascending infection and stone formation are the shortening of the period of recumbency and maintaining the general health of the patient Once a stone has been formed it must be removed before further progress is possible This usually will require surgery or crushing but success in dissolving small stones is sometimes possible with solution G (Suby Suby and Albright)

If infection occurs with pyrexia sulpha drugs and penicillin should be used It should be remembered that if an infection is difficult to control there is probably a mechanical obstruction and the urinary tract should be investigated

As the bladder begins to develop reflex activity further bladder training should be instituted the aim being to ensure that the bladder capacity is maintained so that when the reflex bladder is fully established the patient will be able to go a full three hours between bladder emptyings This should be started as soon as possible and should not be left till the patient begins to get up Not only is this advantageous from the point of view of the bladder but the effect on morale of beginning to get some urinary control is considerable

With the partial lesions the bladder problem is easier and after the same initial phases it should be possible to obtain a normal bladder apart perhaps from a little precipitancy

The Skin

Second only in importance to the urinary tract is the care of the skin The essential factor in causing pressure sores is the ischaemia caused by local pressure This is made more easy in the early stages after cord injury particularly in thoracic injury, by the paralysis of the vasomotor pathways As with the bladder prevention rather than cure should be aimed at but this involves unremitting nursing care from the very first The patient must be moved on a regular hourly routine and in moving extreme care must be taken to ensure that he is rolled and not dragged His bed should be therefore at a height to enable the nursing staff to do this without strain It is most important that he should never lie in a wet bed even for so short a time as fifteen minute Once the skin becomes sodden nothing will save it No form of mechanical splint will replace nursing care and an intact skin can only be maintained by meticulous and constant attention In particular plaster beds which were previously recommended are to be condemned It

is a fact that the worst cases of both contractures and sores have been found in patients treated in this way

Once the skin has broken, numerous local applications have been tried, but in general tincture of benzoin is as useful as any, and relief of pressure and general measures are much more important than local treatment As with the bladder the patient's general health is the most important factor in getting sores to heal It is remarkable how much protein can be lost from a large sore, and how great is the effect of septic absorption from it A patient with a large sore may be reduced to complete cachexia unless steps are taken to prevent this

Even after the patient has begun to sit up, the skin must not be forgotten, and he must be taught to move himself regularly to avoid prolonged pressure on anaesthetic areas

Laminectomy

Opinion is by no means agreed as to either the optimum time to operate or on the choice of case to explore It is agreed that, if the spinal cord is completely divided, nothing can be done to repair this, and operation is only a waste of time Should the x-ray pictures show such a gross abnormality that this is inevitable the decision is easy One of the difficulties is that the initial spinal shock will mask an incomplete lesion, and it is necessary to wait till this has passed off before knowing whether there is a complete transverse lesion present It is because of this that many neuro-surgeons consider that immediate exploration is desirable, that it may do good, as for instance if there is a fragment of bone driven into the cord, and should not, in expert hands do harm If at the same time stout tibial grafts are inserted, subsequent nursing is made materially easier

The more conservative surgeons feel however that this inevitably means that a number of patients are subjected to an unnecessary operation They maintain that there is nothing to be gained by exploring a complete lesion, whether there is a manometric block or not

They recommend that operation should be confined to those patients who have a block, but who show some sign of recovery, and that the leminectomy should be delayed until after the initial spinal shock is passing off, about 7 to 10 days usually Thus Munro (1945) recommends that, if the initial lumbar puncture shows a block attempts should be made by gentle extension using rolled blankets under the site of

injury to restore the patency of the subarachnoid space and only recommends exploring when it is clear that these measures are failing to improve the block

In view of these conflicting opinions it is difficult to lay down any rule but it is stressed that early exploration demands expert neurosurgery if damage is to be avoided and should only be considered when this is available

General Management

It must be recognized that when a patient with a spinal cord lesion is admitted a prolonged stay in hospital will be involved that it is likely that he will develop debilitating infections either skin or urinary and that the sudden conversion of a young and active adult to a bed ridden and helpless patient involves a profound emotional shock

The effect of his general condition on the recovery of his spinal cord his bladder and his skin has been stressed above, and it will be realised how much they are interdependent From the first therefore nutrition must be watched and in particular the protein intake as even apart from the loss involved by infections of skin or urine these patients tend to hypoproteinaemia It is advisable to make periodic blood estimations so that this may be corrected if necessary by intravenous transfusions A full diet of vitamins salt and fluids also must be given

Physiotherapy has also a considerable part in treating these cases passive movement should be begun from the first to prevent contractures and stiffness of the joints In later stages it is one of most useful *measures in controlling flexor spasms* and once the degree of permanent disability can be assessed then exercises to train and re-educate the *muscle power left to the patient can be started*

Occupational therapy is most useful and should even while the patient is in hospital merge into vocational training as many of these patients will have to change their occupation to one suited to their disabilities

There is much to be said for treating these patients in special centres as has been done to a considerable extent for the recent war casualties This enables the most economical use to be made of the trained staff and it will be appreciated from what has been said above that a high standard of special training is needed for these patients It is also a great advantage *for the recently injured to be able to see to what a considerable extent similar disabilities to theirs can be overcome*

It should always be remembered that it is easy for the patient to slip into an apathetic and hopeless condition and not to realise how much he can do even with a complete lesion towards living a completely self supporting life He must be encouraged from the first to appreciate that his part is to be an active one and that he must not just wait patiently for improvement It is perhaps not out of place here to enjoin the same attitude on the medical staff It is easy to lose heart over these long cases and it is difficult to believe how much can be done until one has actually seen some of the results of modern methods of treatment and rehabilitation

Late Treatment

In the severe case a stage may be reached in which further progress is prevented by the development of severe flexor spasms the classical paraplegia in flexion and mass reflex The slightest stimulus to the paralyzed parts whether intrinsic from, for instance, distension of bladder or bowel or extrinsic from any jolt or even change of temperature may produce a violent spasm of the legs with emptying of the bladder and at times the bowel too This condemns the patient to a bed-ridden sodden existence in which no amount of nursing care can prevent bed sores occurring, an additional source of stimuli for further spasm As this state continues contractures in flexion soon develop and are very difficult to deal with as any type of splint or restraint defeats its aim by again producing more spasms

Much may be done for these cases by the early institution of regular passive movements, particularly if carried out in a continuous bath by standing exercises between parallel bars and by careful avoidance of all possible stimuli, particularly urinary sepsis and bed sores

Despite these precautions, however, some cases are unmanageable and for these surgical measures have been devised to convert the spastic paraplegia into a flaccid one by destroying the anterior roots from T 10 or 11 to S 1 This may be done either by alcohol injection or by surgical division The result in carefully selected cases may be to convert the helpless, wet bed ridden patient into one who is ambulant with adequate splints and has complete bladder control Further experience with these measures is necessary however, before final assessment is possible but the results so far are encouraging

Special Points Relative To Various Areas

Cervical Region

Of the immediate severe lesions only those below C 4 will live to *come to hospital Even below this level the only muscle of respiration* left is the diaphragm and respiratory embarrassment may be a serious complication so much so that three quarters of the deaths in lesions of this region are due to respiratory failure and in the initial stage this may take precedence over all other factors As well as the ordinary measures such as the administration of oxygen it is important to avoid anything which will increase the embarrassment of the diaphragm and in particular abdominal distention must be avoided

Few of the complete lesions in this region will survive the first week so that in comparison with the lower lesions the bladder and skin are less serious problems On the other hand however the paralysis of the hands with the associated wasting of the small muscles brings difficulties of its own into the picture

If the joints and small muscles of the hands are neglected the lack of movement and the wasting are apt to lead to permanent changes and the result may be that even though the spinal lesion recovers full function never returns to the hands To prevent this physiotherapy should be started as early as possible Munro (1943) also emphasizes the importance of keeping up the general nutrition particularly the vitamins and has found that carefully given diathermy to the great vessels of the neck is useful

In patients who have sustained a head injury it is easy to overlook an associated cervical cord injury The type of injury is typically a blow on the head when the neck is flexed for example a car or plane crash when the patient is thrown forwards striking his head on the wind screen The general disturbance and unconsciousness may mask the spinal cord injury typically at C 5 or 6 Walshe (1936 1944) has emphasized particularly how easy it is to misinterpret these minor injuries It is often only later when the patient is again up and about that he complains of some pain in the neck stiffness and clumsiness of the legs and weakness and wasting of the small muscles of the hands In these cases the sensory loss is frequently minimal and if overlooked may lead to the erroneous conclusion that the spinal condition is independent of the injury In these cases inversion of the supinator jerk may be found that is when the elicitation of the supinator jerk evokes a flexion of all the fingers exceeding in briskness the normal jerk

Thoracic Region

Munro (1940) has suggested that interference with the vasomotor outflow in lesions of this area renders even more likely the occurrence of bed sores Particular care should, therefore, be taken of skin in lesions at this level

Lumbar and Sacral Region

These are at first almost indistinguishable clinically from lesions of the cauda equina (see Chapter XVIII of the volume) at a later stage If the lesion is in the lumbar region spasticity may develop in the portions of the lower limbs innervated from the part of the cord below the lesion the ankle jerks becoming exaggerated and the plantar reflexes extensor Sacral cord injuries rarely can be differentiated from injuries of the cauda equina

Meningitis Circumscripta Serosa (Spinal Arachnoiditis)

Among the possible later sequelae of trauma to the spinal cord, there may occur a thickening of the pia-arachnoid and even dura with cyst like pockets filled with cerebrospinal fluid The original injury may have apparently caused no nervous injury, or there may have been symptoms for a time, which cleared up completely prior to the development of the arachnoiditis The interval may vary from a few weeks to over 20 years In many cases the lesion appears to arise for other reasons, and trauma is only one of the causes of this peculiar condition Clinically the picture varies considerably, and any part of the spinal cord and cauda equina may be affected, but typically the cases start either with spontaneous pain or with symptoms of spinal compression The pain begins usually as a root pain but later may spread to involve wide areas (Elkington, Hinds Howell) Other cases may be indistinguishable from spinal tumours but in many, curious anomalies in reflex activity are to be found, an absent ankle or plantar reflex in a case of spastic paraplegia and in general sphincter disturbances only come on late in these patients In certain cases the radiological appearances after opaque oil may be quite distinctive the oil being held up in a series of droplets classically likened to the guttering of a candle

The results from surgery vary If the cyst formation is well localized,

or if the arachnoid adhesions are limited as may be the case to a single band they may do extremely well In the patients with more extensive lesions, particularly those in whom the symptoms have been present for a long time and where there are obvious cord changes seen at operation the results are disappointing

Protrusion of the Intervertebral Disc

In the less severe cases of trauma to the vertebral column the bony components may escape injury and the stress fall on the intervertebral discs This is particularly true of the less dramatic forms of accident jolts or strains which may pass almost unnoticed sustained for instance while lifting a heavy weight which slips suddenly in playing games or in doing physical training The result of these may be to cause a fracture of the annulus and, after often a considerable latent period the central part of the disc, the nucleus pulposus may extrude itself and press either on the cord or more frequently on the nerve roots

The commonest area in which this occurs is the lumbosacral region (see Chapter in this volume on cauda equina lesions) but of recent years it has been recognized to be not uncommon in the cervical region If the protrusion is centrally placed it may compress the cervical region of the cord giving rise to a paraplegia, usually not complete and often characterized by signs predominately motor with little and patchy sensory loss If the history of trauma is overlooked the case may easily be mistaken for a system degeneration as these patients progress slowly and may remain stationary once the protrusion has occurred The Queckenstedt s test may not show an absolute block and the increase in protein may be only slight but in many help may be got from the x-rays which often show a narrowing of the intervertebral space It is important not to miss these lesions as these patients respond very well to surgical removal of the protruded disc

The clinical picture associated with the lateral protrusions has been fully recognized comparatively recently (Spurling and Scoville Elliott and Kraemer) and it is only now that it is being appreciated that this condition is by no means rare The discs involved are almost exclusively the 5th and 6th cervical with the 6th considerably the more common of the two As with root pressure elsewhere the presenting feature of these patients is pain In the past they have been regarded as brachial neuritis and their recognition has helped considerably to clarify this mixed group of cases

Thoracic Region

Munro (1940) has suggested that interference with the vasomotor outflow in lesions of this area renders even more likely the occurrence of bed sores Particular care should, therefore, be taken of skin in lesions at this level

Lumbar and Sacral Region

These are at first almost indistinguishable clinically from lesions of the cauda equina (see Chapter XVIII of the volume) at a later stage If the lesion is in the lumbar region, spasticity may develop in the portions of the lower limbs innervated from the part of the cord below the lesion the ankle jerks becoming exaggerated and the plantar reflexes extensor Sacral cord injuries rarely can be differentiated from injuries of the cauda equina

MENINGITIS CIRCUMSCRIPTA SEROSA (SPINAL ARACHNOIDITIS)

Among the possible later sequelae of trauma to the spinal cord there may occur a thickening of the pia arachnoid and even dura with cyst like pockets filled with cerebrospinal fluid The original injury may have apparently caused no nervous injury, or there may have been symptoms for a time, which cleared up completely prior to the development of the arachnoiditis The interval may vary from a few weeks to over 20 years In many cases the lesion appears to arise for other reasons, and trauma is only one of the causes of this peculiar condition Clinically the picture varies considerably, and any part of the spinal cord and cauda equina may be affected, but typically the cases start either with spontaneous pain or with symptoms of spinal compression The pain begins usually as a root pain but later may spread to involve wide areas (Ellington, Hinds Howell) Other cases may be indistinguishable from spinal tumours but in many, curious anomalies in reflex activity are to be found, an absent ankle or plantar reflex in a case of spastic paraplegia, and in general sphincter disturbances only come on late in these patients In certain cases the radiological appearances after opaque oil may be quite distinctive, the oil being held up in a series of droplets classically likened to the guttering of a candle

The results from surgery vary If the cyst formation is well localized,

intervertebral space and oblique views may show a narrowing of the intervertebral foramen with proliferation of bone in the foramen It is possible also to outline the protrusion or to show the occlusion of the foramen with opaque oil but this is unnecessary as the clinical signs localize the lesion so exactly

The great majority of these patients will respond well to conservative measures Simple rest in bed with the neck adequately supported is enough for many of them the more resistant may need gentle head traction or a supporting collar With these measures the recovery is much better than with the lumbar cases and only a small minority will need surgery

BIBLIOGRAPHY

BROWN SEQUARD C E Lancet 1869 I 65 1 1 33 401 457
ELKINGTON J ST C Brain 1936 LIX 181
ELLIOTT F A and KREMER M Lancet 1945 I 4
GUILLAIN G and BARRE J A Ann de l Med 1917 IV 598
GUTTMANN L Med Times New York 1943 LXXIII 318
HEAD H and RIDDOCH G Brain 191 XL 188
HEAD H and THOMSON T Brain 1906 XXIX 537
HINDS HOWELL C M Proceed Roy Soc Med 1936 XXX 33
HOLMES G Brit Med Jour 1915 II 397
JEFFERSON G Trans Am Neurol Assoc 1943 101
LHERMITTE J Rev Neurol 1919 XXXI 03
MUNRO D New Eng Jour Med 1940 CCXXIII 391 194 CCXXIX 919 1945 CCXXXIII 453 1946 CCXXXIV 07
RICHES E W Lancet 1943 II 1 8
RIDDOCH G Brain 1917 XL 64 Lancet 1918 II 839
SHERRINGTON C S Brain 1915 XXXVIII 191 Integrative Action on the Nervous System 1906
SPURLING R G and SCOVILLE W B Surg Gynec and Obstet 1944 LXXVIII 350
SUBY H I SUBY R M and ALBRIGHT F Jour Urol 194 XLVIII 549
WALSHE F M R Brain 1914 15 XXXVII 69
WALSHE F M R Lancet 1944 II 173
WALSHE F M R and ROSS J Brain 1936 LIX 7

September 1 1948

In contrast to the disc lesions in the lumbar region it is comparatively rare to get a definite history of trauma in these patients, and it has been suggested that degenerative changes are in some the cause of the protrusion It must be noted however, that they occur almost exclusively at the typical area for lesions due to indirect force which makes it difficult to believe that trauma plays no part in their production It may be that the potent factor is multiple minor injuries rather than a single incident

In the cervical region the nerve roots correspond in number with vertebra below, that is the 6th cervical root comes out between 5th and 6th vertebra at the level of the 5th disc and the 7th root at the level of the 6th disc They leave the cord at right angles and lie directly over the intervertebral disc so that a protrusion from the disc can easily compress the nerve root without affecting the spinal cord

Clinically, while some of these patients start with pain and stiffness in the neck, this is often short lived, and in general the pain in the arm dominates the picture This radiates from the shoulder down the arm and outer side of the forearm into the hand the 5th disc lesions involving the thumb, while the 6th affect chiefly the first finger but may spread to the second finger and tip of the thumb This pain is intensified by any sudden jolt or jerk and also becomes worse, if the patient stays in one position too long, thus at night they will get up and walk about to relieve the pain

One of the most characteristic features on examination of these cases is that the pain is exaggerated by pressure on top of the head when the neck is flexed to the side of the pain Percussion over the lower cervical spine may also reproduce the pain In the arm the signs will depend on which disc is affected The 5th disc lesions pressing on the 6th nerve root give rise to weakness and later, wasting of the biceps with absence of the biceps jerk In some cases this is associated with impairment of sensation over the dorsum of the thumb and radial side of the wrist With the 6th protrusions the muscle chiefly affected is the triceps, although there may also be some weakness of the extensors of the wrist and fingers The sensory loss lies more medially involving the 1st and 2nd fingers and running up the forearm but in both lesions the amount of sensory loss varies considerably and is much less than the subjective complaints might suggest as the patients often complain of widespread numbness of hand and forearm

In a fair proportion of these patients the diagnosis can be clinched by the x-ray findings This typically will show narrowing of the affected

CHAPTER XVIII

LESIONS OF THE CAUDA EQUINA AND CONUS MEDULLARIS

By N S ALCOCK

TABLE OF CONTENTS

TYPES OF LESION

The cauda equina and conus medullaris may in common with the rest of the spinal cord be involved in trauma to the surrounding bony structures Such lesions as fracture dislocations of the lumbar vertebrae or fractures of the sacrum are apt to damage the contents of the spinal canal or, as with the sacrum where the fracture usually runs through the intervertebral foramina to injure the nerve roots as they emerge[1] Intraspinous tumours metastatic deposits gummata or meningeal syphilis also occur in this area or the nervous elements may be involved in bone infections whether by tubercle or pyogenic organisms

Apart from these however the cauda equina may be affected by a group of conditions which are largely peculiar to it By far the commonest of these is the posterior protrusion of the intervertebral disc

CHAPTER XVIII

LESIONS OF THE CAUDA EQUINA AND CONUS MEDULLARIS

By N S ALCOCK

TABLE OF CONTENTS

TYPES OF LESION

The cauda equina and conus medullaris may in common with the rest of the spinal cord be involved in trauma to the surrounding bony structures Such lesions as fracture dislocations of the lumbar vertebrae or fractures of the sacrum are apt to damage the contents of the spinal canal or as with the sacrum where the fracture usually runs through the intervertebral foramina to injure the nerve roots as they emerge[1] Intraspinous tumours metastatic deposits gummata or meningeal syphilis also occur in this area or the nervous elements may be involved in bone infections whether by tubercle or pyogenic organisms

Apart from these however the cauda equina may be affected by a group of conditions which are largely peculiar to it By far the commonest of these is the posterior protrusion of the intervertebral disc

Although not strictly limited to the lumbar region this lesion is much more common here than elsewhere in fact it outnumbers considerably all the other affections of the cauda equina

Again, because this is the region in which a lumbar puncture is done, the nervous elements may be involved if, fortunately rarely, complications arise from this procedure Particularly is this so if some potentially irritating substance such as penicillin or a spinal anesthetic is injected Since this area is the most dependent part of the cerebrospinal fluid reservoir any foreign substance in the cerebrospinal fluid will tend to gravitate here Thus symptoms of lumbar or sacral root irritation may arise during recovery from a subarachnoid hemorrhage, or after opaque oil has been injected higher up The same may occur during or after meningitis from the infection settling in this site

Some forms of encephalomyelitis also seem to attack the conus particularly, thus not uncommonly post measles encephalitis may leave a tiresome sphincter weakness as a sequel

General Features

Consequent on the anatomical differences between the cauda equina and the rest of the spinal cord lesions here have certain general features as distinct from the syndromes higher up The spinal cord fills nearly the whole of the vertebral canal and a lesion there tends to compress the whole of the cord more or less generally and so gives rise to a symmetrical picture In the cauda equina however, the nerve roots are floating in the cerebrospinal fluid and are relatively further apart so that not only may one leg escape while the other is severely affected but also the motor and sensory roots may be differently affected

Pain—As the cauda equina is made up entirely of nerve roots it is perhaps not surprising that pain is typically one of the most prominent and distressing symptoms This is true not only of the irritative lesions where it might be expected, but also of the compressions whether by tumour or disc, in which pain is not only the presenting symptom but usually the most prominent throughout It is a feature too of the traumatic cases and may date almost from the moment of injury or appear much later as a manifestation of recovering function

The pain typically is in a root distribution and may be either spontaneous or arise only after mechanical stimulation Particularly if due to pressure it is made worse by any sudden jolt or movement or by

coughing or sneezing The pain tends to be worse at night and often prolonged maintenance of any one posture is difficult even that of lying and the patients will get up and walk the room to get relief A number of these patients say in fact that the pain is easiest when walking and that either sitting or lying will make it worse

The Bladder and Rectum—Sphincter disturbances particularly of the bladder but also to some extent of the bowel form a large part of the symptomatology of lesions in the cauda equina and conus region In fact with lesions of the tip of the conus the loss of sensation and power may be of little account and the bladder may be the outstanding problem In some ways particularly in the complete lesions the handling of the bladder may be more difficult than with the spinal lesions and it may be helpful to review shortly the behaviour of the bladder

The bladder is innervated from two levels of the cord from the lower thoracic and upper lumbar level via the hypogastric nerves and from the 2nd 3rd and 4th sacral segments via the pelvic and pudic nerves From the practical point of view however the hypogastric nerves may be disregarded apart from possibly carrying some sensory fibres their function is negligible and no difference will be found with lesions above or below their level of origin[2 3 4]

The initial stage after a sudden destructive lesion of the sacral area of the cord or of the roots coming from it is the same as is found in the state of spinal shock The bladder acts purely as an elastic bag and the sphincter is tightly shut It is in the later stages that the difference from spinal lesions becomes apparent In lesions higher up the bladder passes through the autonomous stage to reach the fully automatic or reflex bladder which may hold a reasonably large amount of urine and empty itself completely with a powerful contraction and which may with care be quite compatable with a dry ambulant life In lesions in which the pelvic and pudic nerves are involved the bladder is separated from all connection with the spinal centers and this is also the case when the bladder center in the cord is involved in the destructive process In this case the function of the bladder is dependent on the intramural plexus of nerves and ganglia and the function never progresses beyond the autonomous stage and is much slower in reaching this stage than when the spinal reflexes are intact In fact the longer the length of healthy cord (below the lesion) the better is the reflex behaviour of the bladder[2] Even when the autonomous bladder is established the reflex micturition is not nearly so efficient as with the so called automatic bladder The bladder reacts to a much smaller filling

and the contraction is poorly sustained and often leaves a quantity of residual urine While in certain patients this state of affairs may be not too unsatisfactory, there is a tendency for the bladder never to become properly distended and therefore, gradually to undergo contracture of the muscle so that the capacity slowly shrinks until finally the regrettable result may be an almost continuous dribbling incontinence, for which there is no alternative but the wearing of a urinal Even if this does not occur the presence of residual urine is most undesirable and means that there is a continual threat of infection, and that infection, when it occurs is most difficult to control

This then is the problem, which presents in the management of the cauda equina bladder and one which so far has not been adequately solved Correct management in the early stages however, may help to prevent the worst feature of this progression

Initially in the stage of the atonic bladder the paramount aim is to prevent infection as on this the patient's life may well depend and while infection is present any hope of reasonable micturition is in vain Modern methods of chemotherapy have helped greatly in this and have therefore, thrown more emphasis on the second aim which it to maintain a bladder of normal size neither allowing over distention to occur nor letting the bladder shrink Neither ordinary catheterisation nor a suprapubic cystotomy can achieve this and it can be realised only by some method of tidal drainage either through a leak-proof catheter inserted high up on the bladder wall or through an urethral catheter As stated above the development of autonomous micturition is slower in these lesions and one must be prepared to persist in tidal drainage for often considerably longer than with lesions higher up

Various measures have been tried to deal with the undesirable end results such as clipping an in dwelling catheter or even putting a clip onto the urethra itself but so far it remains a problem for which there is no satisfactory answer

PROTRUDED INTERVERTEBRAL DISC

It is now well known that it is not uncommon for the annulus of an intervertebral disc to rupture and allow the nucleus pulposus to extrude and involve one or more of the elements of the cauda equina The commonest discs to be affected are the lower lumbar or lumbosacral ones and since this has become popularly appreciated, a considerable

volume of work has been done on the subject many aspect of which are outside the scope of this chapter It is however by far the commonest lesion to affect the cauda equina and will illustrate well many of the general points already referred to

Pain is thus almost invariably the presenting feature Because of the localisation the pain is generally in the sciatic distribution i e it runs from the back to the buttock down the back of the thigh outer side of the leg around the lateral malleolus and along the outer side of the foot to involve the lateral toes It should be remembered however that a different localisation modifies this distribution Although the lesion is confined to within the spinal canal it is typical of the condition that the sciatic nerve is tender both to pressure and stretching often as far down as the knee a phenomenon not adequately explained by the anatomical lesion but possibly dependent on the edema which affects the nerve roots compressed by the protrusion Partly because of this and partly because of the rigidity of the spine the pain is made worse by any posture which causes this stretching or pressure on the nerve so that the patients are unable to bend down or sit in comfort Their best position is to lie in bed with the affected limb uppermost flexed slightly at knee and hip Any sudden movement and in particular coughing or sneezing brings on an acute exacerbation

In the majority of patients the sensory and motor signs are less in evidence than the pain but a proportion of them show weakness and wasting of the muscles supplied by the root affected with consequent reflex changes and there may be sensory impairment over the dermatome concerned Dependent on the size and site of the protrusion more than one root may be involved and a certain number of these patients present the typical picture of a complete middle cauda equina lesion with bladder disturbance and bilateral signs These cases may be indistinguishable from new growths in the same area a point which illustrates the axiom that neurological signs only localise and can not differentiate between one pathological lesion and another

One of the most typical features of these patients is the tendency to remissions and relapses The reason for this is still not fully understood It seems unlikely that the protruded portion of the disc retracts and as Falconer and associates[5] have shown this need not accompany a remission It seems more probable that the associated edema of the disc and root settles down or that the root slips off the protrusion and so relieves the pressure Whatever the explanation the clinical fact sometimes is forgotten when considering treatment It should be remembered

and the contraction is poorly sustained and often leaves a quantity of residual urine While in certain patients this state of affairs may be not too unsatisfactory there is a tendency for the bladder never to become properly distended and therefore, gradually to undergo contracture of the muscle so that the capacity slowly shrinks, until finally the regrettable result may be an almost continuous dribbling incontinence, for which there is no alternative but the wearing of a urinal Even if this does not occur the presence of residual urine is most undesirable and means that there is a continual threat of infection, and that infection when it occurs is most difficult to control

This then is the problem which presents in the management of the cauda equina bladder, and one which so far has not been adequately solved Correct management in the early stages however, may help *to prevent the worst feature of this progression*

Initially, in the stage of the atonic bladder, the paramount aim is to prevent infection, as on this the patient's life may well depend, and while infection is present any hope of reasonable micturition is in vain Modern methods of chemotherapy have helped greatly in this and have therefore, thrown more emphasis on the second aim which it to maintain a bladder of normal size neither allowing over-distention to occur nor letting the bladder shrink Neither ordinary catheterisation nor a suprapubic cystotomy can achieve this and it can be realised only by some method of tidal drainage either through a leak proof catheter inserted high up on the bladder wall or through an urethral catheter As stated above, the development of autonomous micturition is slower in these lesions and one must be prepared to persist in tidal drainage for often considerably longer than with lesions higher up

Various measures have been tried to deal with the undesirable end results such as clipping an in dwelling catheter or even putting a clip onto the urethra itself, but so far it remains a problem for which there is no satisfactory answer

Protruded Intervertebral Disc

It is now well known that it is not uncommon for the annulus of an intervertebral disc to rupture and allow the nucleus pulposus to extrude and involve one or more of the elements of the cauda equina The commonest discs to be affected are the lower lumbar or lumbosacral ones and since this has become popularly appreciated, a considerable

Complete Form

When all the spinal roots composing the cauda equina are injured the terminal portion of the spinal cord is of necessity involved also There is complete flaccid paralysis of the lower extremities and abolition of the tendon plantar and cremasteric reflexes If the lesion is high enough to allow the conus to escape destruction it may be that the anal and bulbocavernosus reflexes are retained but this is unusual and

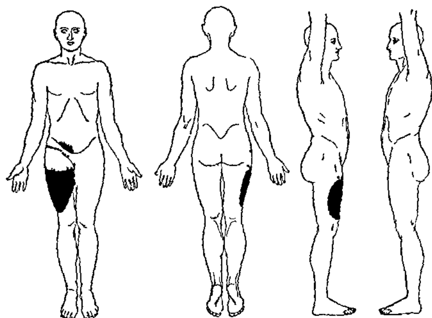


FIG 2.—The dotted line bounds the area of over reaction to pin prick and within th area colored black the skin was insensitive to light touch pin prick and heat and cold The author expresses his indebtedness to the late Dr George Riddoch for this illustration.

it is general for them also to be unobtainable The area of sensory loss which includes the external genitalia and the urethra is represented in Fig 1

Normal vesical sensibility is abolished although the patient may be aware that the bladder is full from the sensation of abdominal distention Some patients may complain also of unpleasant sensations just before

that before the cause was known it was well recognised that sciatica was a condition which tended to recover spontaneously and our knowledge of the pathological lesion does not alter the clinical course of a disease

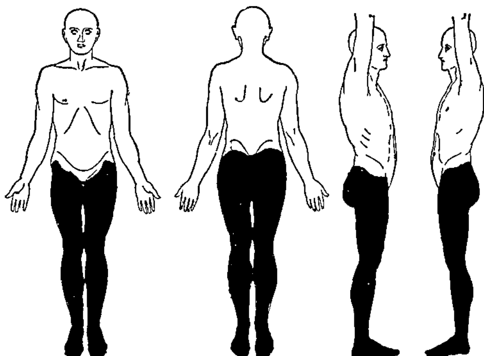


Fig 1 —Complete cauda lesion To represent the area of sensory loss The author expresses his indebtedness to the late Dr George Riddoch for this illustration

There is no doubt however that in the appropriate case a surgical removal of the protruded portion of a disc can give dramatic relief and that relapses certainly are less frequent after surgery Sufficient time has not yet elapsed since surgical treatment has been widely used to allow an adequate assessment of the final results, and at present each case must still be considered on its merits

Clinical Types

It is convenient for clinical description to recognise certain forms of paralysis due to injury of the cauda equina at different levels

Complete Form

When all the spinal roots composing the cauda equina are injured the terminal portion of the spinal cord is of necessity involved also There is complete flaccid paralysis of the lower extremities and abolition of the tendon plantar and cremasteric reflexes If the lesion is high enough to allow the conus to escape destruction it may be that the anal and bulbocavernosus reflexes are retained but this is unusual and

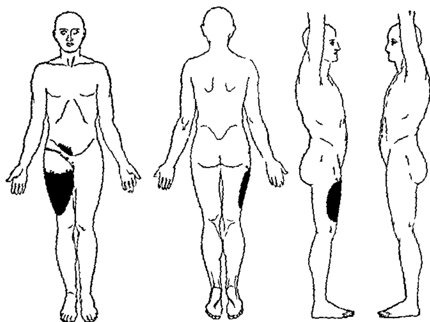


FIG 1—The dotted line bounds the area of over reaction to pin prick and within the area colored black the skin was insensitive to light touch pin prick and heat and cold The author expresses his indebtedness to the late Dr George Riddoch for this illustration

it is general for them also to be unobtainable The area of sensory loss which includes the external genitalia and the urethra is represented in Fig 1

Normal vesical sensibility is abolished although the patient may be aware that the bladder is full from the sensation of abdominal distention Some patients may complain also of unpleasant sensations just before

passing water, which Denny Brown[3] has shown to be associated with vesical contractions, and which probably are appreciated through the hypogastric nerves In many cases, however, even though these nerves are intact, there is no sensation from the bladder at all

Upper Caudal Form

In this form the upper lumbar roots are chiefly affected and usually on one side only It is most frequently the end result of trauma and is

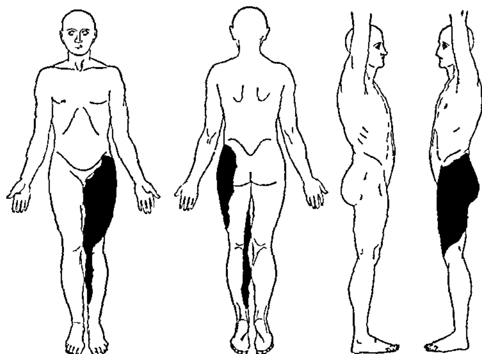


Fig 3—The area of anesthesia and analgesia is represented in a case in which the first second third and fourth lumbar roots on the left side were injured by a rifle bullet The author expresses his indebtedness to the late Dr George Riddoch for this illustration

preceded by an initial phase of complete paralysis The chief weakness is in extension of the knee, and usually the sphincters recover sufficiently not to be troublesome Figs 2 and 3 illustrate the anesthesia left finally after a gun shot wound of the 3rd lumbar vertebra

Middle Caudal Form

The injury falls most heavily on the lower lumbar and upper sacral roots The knee jerks may be retained but the ankle jerks are abolished The muscles below the knee with the possible exception of the tibialis anticus are paralysed and the hamstrings and glutei are weak The areas of sensory loss have a regional distribution as in Fig 4 and vesical rectal and sexual functions usually are more or less impaired

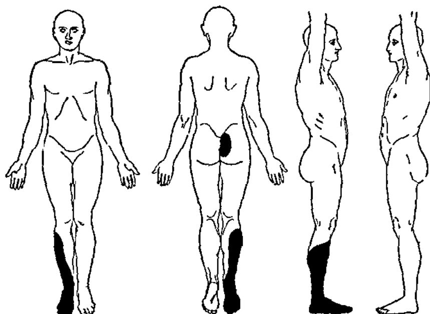


Fig 4 —The areas colored black represent the extent of the sensory loss in a patient in whom the fifth lumbar first and fourth and fifth sacral roots on the right side were injured by a piece of shell the fragment of metal was removed from the body of the fourth lumbar vertebra The author expresses his indebtedness to the late Dr George Riddoch for this illustration

This is the form which usually is produced by a protrusion of an intervertebral disc although as in general only one root is involved the sensory loss is not as complete as in the illustration the saddle area is not involved and the sphincters are not affected As already mentioned however a massive protrusion may cause the complete picture

passing water, which Denny Brown[8] has shown to be associated with vesical contractions, and which probably are appreciated through the hypogastric nerves In many cases, however, even though these nerves are intact, there is no sensation from the bladder at all

Upper Caudal Form

In this form the upper lumbar roots are chiefly affected and usually on one side only It is most frequently the end result of trauma and is

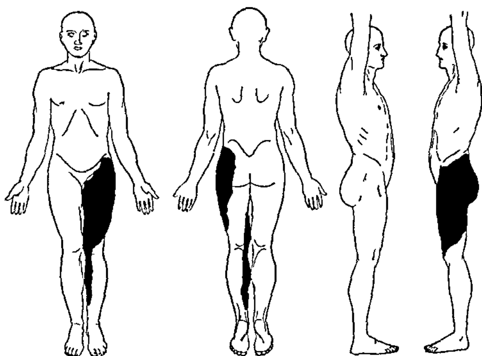


FIG 3 —The area of anesthesia and analgesia is represented in a case in which the first, second third and fourth lumbar roots on the left side were injured by a rifle bullet The author expresses his indebtedness to the late Dr George Riddoch for this illustration

preceded by an initial phase of complete paralysis The chief weakness is in extension of the knee, and usually the sphincters recover sufficiently not to be troublesome Figs 2 and 3 illustrate the anesthesia left finally after a gun shot wound of the 3rd lumbar vertebra

Diagnosis

The conditions which produce the clinical picture of the cauda equina and conus medullaris affections illustrate well the basic principle that *the signs and symptoms of neurological dysfunction only illustrate* the site of the lesion The pathological nature of the lesion must be deduced from other features of the case In reaching a complete diagnosis all the points of the case must be considered and in certain cases

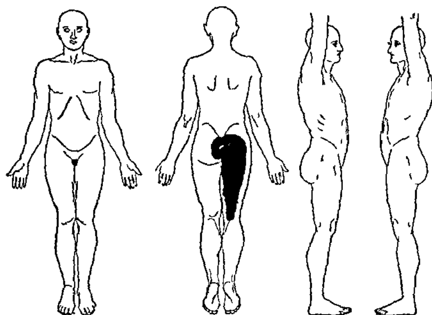


Fig 6 —Represents the area of sensory loss in a case in which the second third fourth and fifth sacral roots on the right side and the fourth and fifth sacral roots on the left side were injured The author expresses his indebtedness to the late Dr George Riddoch for this illustration

only an actual inspection will reveal the true answer For instance while a relapsing history with exacerbations brought on by trauma, is typical of the picture of a protruded intervertebral disc certain cases of new growth within the vertebral canal may give an identical story and the fact that the symptoms come on first after an injury is not incompatable with a tumor

Lower Caudal Form

This form may be produced either by lesions of the sacrum as in Figs 5 and 6 or by a lesion at, say, the 1st lumbar vertebra, in which originally both the nerve roots and the conus medularis was involved, and the nerve roots have recovered but the conus has not In this the knee and ankle jerks may be *normal and the motor loss confined to the* perineal and levator ani group Paralysis of the vesical, rectal and sexual

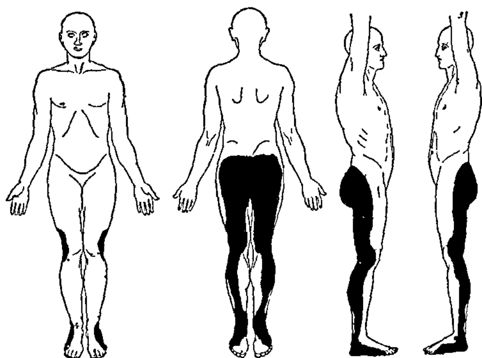


Fig 5 —Bullet wound of the sacral region The area which is colored black represents the extent of the anesthesia and analgesia following injury of all the sacral roots The dotted line bounds an area within which light tactile stimuli were appreciated imperfectly sensibility to pin prick was not affected This dissociation indicates that the lower end of the cord was also damaged The author expresses his indebtedness to the late Dr George Riddoch for this illustration

functions form the outstanding disability and with lesions of slow development as from tumors are often the presenting symptom thus contrasting with the other caudal forms where pain generally is the first complaint

Treatment

In general the treatment of lesions in this area follows that appropriate to other areas Of the special conditions the question of operation on disc cases has been considered The traumatic cases fortunately tend to recover spontaneously better than injuries higher in the spinal column If however, there is reason to believe that the injury has caused a considerable amount of bleeding, the desirability of an early exploration and removal of the blood should be seriously considered If this is left to organise, the consequent fibrosis may involve the nerve roots and give rise to troublesome effects in the later stages of recovery by which time relief by operation may be impossible

BIBLIOGRAPHY

1 BONNIN J G Sacral fractures and injuries to the cauda equina Jour Bone and Joint Surg 1945, XXVI, 113
2 DENNY BROWN D and ROBERTSON E G On the physiology of micturition Brain, 1933 LVI 149
3 DENNY BROWN D and ROBERTSON E J The state of the bladder and its sphincters in complete lesions of the spinal cord and cauda equina Brain 1933 LVI, 397
4 HOLMES, G Observations of the paralysed bladder Brain, 1933 LVI 383
5 FALCONER M A McGEORGE M and BEGG A C Observations on the cause and mechanism of symptom production in sciatica and low back pain Jour Neur, Neurosurgery and Psych 1948 XI 13

July 1 1950